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In the February Number of SURGICAL CLINICS of NORTH AMERICA

SYMPOSIUM on ORTHOPEDIC SURGERY

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CASE: 301*

Seven-year-old girl suffers extensive second- and third-degree burns. Shock and hypoproteinemia treated immediately with massive injections of normal human plasma and 5% dextrose solution. Burned areas covered with antibiotic TYRODERM *tyrothricin cream, heal at optimal rate, without infection, permitting early skin graft.*

THE PATIENT, a seven-year-old girl, was admitted to the hospital suffering from severe second- and third-degree burns. The child's dress had caught fire while she was playing near an open hearth.

Examination revealed first-, second- and third-degree burns over much of the patient's body, face and arms. On the left flank, left side of the chest, mid and posterior axillary region and upper portion of left arm the skin was hard and black. The patient's condition was poor and she was in a state of vital depression.

Burned area heals in 14 days, without infection.

The patient was perspiring profusely, respirations were rapid and shallow, and the pulse was recorded as 112, and thready. Shock and hypoproteinemia were countered immediately by intravenous injection of 750 cc. of five-percent dextrose solution, followed by 500 cc. of normal human plasma. The entire burned area was then carefully debrided and completely covered with antibiotic TYRODERM tyrothricin cream as a precaution against secondary infection.

The next day the child's condition was fair. An additional 1,750 cc. of plasma and 1,000 cc. of five-per-cent dextrose solution were administered. TYRODERM tyrothricin cream was applied again to the entire burned area.

TYRODERM® Tyrothricin Cream is remarkably effective in local treatment of contaminated wounds and burns, ulcers of extremities, and gram-positive skin infections. Greaseless, water-washable, and nonirritating, TYRODERM Cream does not cause skin sensitivity. Contains 0.5 mg. (500 micrograms) of antibiotic tyrothricin per gram. Supplied in 1-oz. tubes and 1-lb. jars. A 1-oz. tube of *Tyroderm* for clinical use will be sent on request from: *Professional Service Dept., Sharp & Dohme, P. O. Box 7258, Philadelphia. 1, Pa.*

By the third day the patient's condition was much improved. The burned area was healing satisfactorily and without evidence of infection. Intravenous administration of fluids and topical application of TYRODERM were continued. As the patient steadily improved, she was able to take sufficient fluid by mouth to render further intravenous therapy unnecessary. In approximately three weeks, skin was grafted successfully to the burned area. TYRODERM tyrothricin cream was again used to prevent secondary infection, and the graft healed at the optimal rate, without complications or undue scarring. Normal motion of the affected arm was restored, cosmetic results were considered satisfactory, and the patient was discharged the thirty-second day after admission.

*Actual case record.

Anesthetic Procedures in the Diagnosis and Treatment of Disease

CHARLES F. McCUSKEY[1] AND HARRY BROWN[2]

UNIVERSITY OF SOUTHERN CALIFORNIA SCHOOL OF MEDICINE, LOS ANGELES

World War II was instrumental in causing surgeons and physicians in general to realize the benefits to be gained from the trained physician-anesthetist in the administration of anesthesia. Some members of the medical profession are still not fully aware of the many ways in which the anesthesiologist can help in the treatment of patients other than by administering surgical anesthesia. It is my purpose to bring to your attention some of the anesthetic procedures which are useful in the diagnosis and treatment of disease. This list is so long that many procedures will be omitted and others mentioned only briefly.

The procedures available for diagnosis and treatment can be divided into the groups listed in Table 1.

Relief of pain is the most common anesthetic procedure performed. There is scarcely a nerve in the body whose impulses cannot be interrupted by the injection of procaine. Experience has demonstrated that the earlier a nerve block is performed, the more effective is the relief. It is first necessary to localize the pain and identify the nerve or nerves involved. The first injections should employ procaine exclusively.

Next to accurate diagnosis, the use of proper solutions is most important in nerve blocking. Procaine in saline solution, in 1 to 2 per cent concentration, may be injected repeatedly with no ill effect on nerve tissues. Intracaine may be used in a similar manner. These same drugs may be used in oil, but with more caution because of the danger of sloughing tissues. Alcohol injections are more prone to complications and should be used only as a last resort or to give prolonged relief. Alcohol neuritis, motor disturbances, and local irritation of sensitive tissues are common complications. Preparations are now available whose essential ingredient is the ammonium radical and which have a selective action upon pain fibers, leaving the motor fibers unaffected.

The sympathetic nerves may be blocked at various sites for intractable visceral pain and circulatory disorders.[1] Acute thrombophlebitis may be effectively treated with lumbar sympathetic blocks. The venous and arterial spasms which produce the pain can be successfully relieved by injecting procaine around the lumbar ganglia.[2] The block can be repeated daily (or more often, if necessary) for two to four days, then every other day until pain and swelling disappear. Even thrombophlebitic process of several weeks' duration and postphlebitic edema will rapidly subside under treatment with sympathetic blocks. Vascular spasm in the legs from other causes can be treated in a similar manner; e.g., vascular spasm due to trauma, exposure to cold, following amputations, ligature of large blood vessels, arterial embolism, and removal of aneurysm.[3]

Swelling and edema of the extremities following fracture and immobilization or operation have been markedly improved by sympathetic blocks. While a definite diagnosis cannot always be made

[1]Associate Clinical Professor of Surgery (Anesthesia), University of Southern California School of Medicine, Los Angeles, California.

[2]Attending staff, Los Angeles County General Hospital and Veterans Administration Hospital, Van Nuys, California.

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TABLE 1

ANESTHETIC PROCEDURES AVAILABLE FOR DIAGNOSIS AND TREATMENT

- NERVE BLOCKING PROCEDURES
  - Subarachnoid (spinal) block
  - Caudal block
  - Sympathetic and paravertebral block
  - Peripheral somatic nerve block
- INTRAVENOUS THERAPY
  - Procaine
  - Curare
- INHALATION THERAPY
  - Oxygen
  - Helium-oxygen
- POSTOPERATIVE COMPLICATIONS AMENABLE TO ANESTHETIC PROCEDURES
  - Thrombophlebitis
  - Pulmonary atelectasis
  - Cerebral thrombosis and spasm
  - Reflex anuria
  - Pulmonary embolus
  - Thyroid crisis

on some cases of postoperative edema, it would appear clinically that the improved circulation is an important factor in reducing the swelling. Certainly any postoperative extremity which is swollen and cool should receive a trial with sympathetic ganglia blocks.

Sympathetic block of the lower extremity[2,4] is used for the diagnosis and surgical evaluation of peripheral vascular disease in which there is vasospasm. If circulation is improved by sympathetic block, surgery of the regional ganglia can be performed and the same improvement will be evident on a permanent basis.

Block of the cervical sympathetic ganglia is performed when the same symptoms or etiologic factors exist in the upper extremity. The cervical sympathetic (stellate ganglion) block is widely used for causalgia type of pain in the arms, the dystrophy and swelling which are sometimes associated with coronary disease (shoulder-hand syndrome[5]), and various ill-defined and vague types of pain which do not fit any particular diagnostic pattern. Volpitto[6] and others have advocated stellate block for the spasm of cerebral vessels which accompanies cerebral embolism and thrombosis. Stellate block has also been used to treat pulmonary embolus with success in some cases.[7]

Our knowledge of the anatomy and function of the autonomic nervous system still has many blank spaces. However, there exists much practical knowledge which can be applied with benefit in certain disease states. Blocking the sympathetic nerves for the treatment of pancreatitis has given striking results in certain cases and is worthy of further application.[8] This can be performed by posterior splanchnic block,[9] or by paravertebral block (fifth to tenth thoracic). The block is not successful in all cases, presumably since not all pancreatitis is on a reflex vasoconstrictor basis, some being on a mechanical basis. Pain may be on the right or left side, depending on whether the body or tail of the pancreas is involved. Since surgical treatment offers little to the patient and conservative management is usually followed, splanchnic block is worthy of trial whenever the diagnosis of pancreatitis is made.

Reflex anuria has been relieved by splanchnic block,[10] spinal anesthesia, and paravertebral block (T11, T12, L1, L2) on the affected side or bilaterally. Reflex anuria on one side may initiate the same process on the other side. Anuria may be due to renal calculus, acute glomerular nephritis, or nephritis of scarlet fever.

Pain from the heart can be relieved by blocking the first to fifth thoracic nerves, inclusive, at the paravertebral position, or the corresponding sympathetic ganglia may be blocked. The usual procedure is to block the nerves with procaine, and if this gives a favorable result one may decide on alcohol injections. Alcohol injections, however, should be reserved exclusively for the poor risk patient with intolerable pain,[1,11] and the failures and complications make it inadvisable for those who can undergo operation.

Although sympathetic block is a simple and harmless procedure, all too frequently it is used as a last resort after a considerable lapse of time following onset of pathology. The injections should be started early and repeated with sufficient frequency to determine whether the disease process will be altered by interruption of sympathetic activity.

While spinal or subarachnoid block is usually associated with surgical anesthesia, its use has been extended to include certain diagnostic and therapeutic procedures. Pulmonary edema[13] has been treated with spinal block on the basis of the decreased venous return to the heart which is produced; in effect, one produces a bloodless phlebotomy. Spinal anesthesia to the fourth thoracic segment (nipple line) will paralyze the sympathetic fibers to the adrenal glands and reduce the

secretion of epinephrine. On this basis it has been used to control the sympathetic overactivity in hyperthyroidism immediately before surgery or in the postoperative crisis.[14]

Spinal block is one of several methods of blocking sympathetic fibers. Sympathetic block by the spinal route[15] produces an ascending segmental paralysis of the vasoconstrictor fibers. This test is used, along with others, to evaluate the operability of the hypertensive patient and to determine the extent of resection of the sympathetic chain necessary to produce a successful therapeutic result. The same test may be performed by injecting the procaine solution into the caudal space and forcing it up into the epidural space to the desired height[16] by use of larger volumes.

The caudal or spinal block can be used to paralyze the sympathetic fibers to the legs. However, the sympathetic ganglia block (or paravertebral block) has the advantages of limiting the extent of the block to a minimum and avoiding sensory and motor changes which usually accompany the spinal or caudal block. If it is necessary to block the sympathetic fibers to both legs, the caudal or spinal route is simpler and less painful to the patient.

The blocking of peripheral nerves for diagnosis and treatment is so comprehensive that it is possible to mention only a few of the more common conditions and nerves involved. The pain and discomfort of herpes zoster along the course of any nerve can be relieved by peripheral nerve block. The intercostal nerves are commonly involved, as are the cervical nerves and branches of the fifth cranial nerve. Intercostal nerve block is frequently used to relieve postoperative incisional pain which has such a disturbing effect on pulmonary ventilation,[17] and to relieve the pain due to fractured ribs.[18] The brachial plexus and its branches are commonly blocked for painful or edematous conditions involving the shoulder joint and upper extremity.

When trauma initiates a chronic cycle of discomfort and disability, local or regional blocks have often proved a valuable measure. Quite frequently one sees ill-defined syndromes of the upper extremity characterized by pain, stiff joints, swelling, and dystrophy, and which may be labeled as arthritis, bursitis, fibrositis (myositis), or neuritis. In some such cases brachial plexus block is effective when stellate ganglion block fails. Since the sympathetic fibers travel in the branches of the brachial plexus, there is no explanation for this result at the present time. The only disadvantage of brachial plexus block is the sensory and motor anesthesia which accompanies it. It may be necessary to repeat the block six to twelve times in order to produce the desired result.

The various branches of the cervical nerves and the fifth cranial nerve are easily blocked for neuralgic afflictions and tic douloureux. Quite often a single block will be sufficient to break the cycle of pain and effect a permanent cure; in other instances it will be necessary to repeat the block with procaine, or with alcohol if the procaine block provides insufficient relief. Alcohol injections should be used only as a last resort because of the profound destructive effect on the nerve and possible complications. The procaine block of the fifth nerve will also help the patient decide whether he wants to have permanent functional disruption of the nerve by block or surgery. Injection of nerves with alcohol should be done only by those trained and experienced in this technic because of the complications which may accompany the injection. These complications will vary with the area of injection and nature of the surrounding tissues.

The sciatic nerve is easily approached for injection, as are the sacral nerves. Every effort should be made to arrive at a diagnosis first, but it often becomes imperative to grant the patient symptomatic relief while this is being done. The variety of pathology which expresses itself as sciatic neuralgia is so manifold that it is particularly important to arrive at a diagnosis.

Various solutions are now available for injection whose essential ingredient is the ammonium ion, and these produce sensory anesthesia of prolonged duration without the annoying motor paralyses which accompany the use of procaine. Ammonium salts abolish neuralgic pain and do not produce any motor weakness or loss of touch, pressure, pin-prick, or temperature sensibility.[19] There is no evidence that the ammonium salts affect the vasomotor components of the sympathetic ganglia or peripheral nerves, nor do they relieve pain of visceral origin.

THE use of nerve block in the intractable pain of malignancy[8,20] could be used to a greater extent with relief to the patient and decreased use of narcotics. The pain is usually difficult to localize and relieve with nerve blocking, but the cases in

which it is applicable have had gratifying results. Pain of purely visceral origin is most difficult to control, since autonomic as well as segmental nerves must be blocked and one must go to levels much higher than those supplying the organ causing the pain. Pain from malignant growths of the face can often be relieved by fifth cranial nerve or cervical nerve block.

When pain develops due to spinal metastases paravertebral block can be performed with favorable results. In cases where the distribution of pain is bilateral or too extensive for single nerve blocking, caudal or spinal block can be utilized. After a test block with procaine to determine the amount of relief obtainable, one can use the ammonium salt (chloride or sulfate) preparations[21,22] (e.g., dolamin) or alcohol. Intraspinal alcohol can be used as a last resort for intractable pain.

The technic of blocking peripheral nerves is well described in several texts[23-25] and need not be repeated. It requires a working knowledge of regional anatomy and nerve distribution and some experience in nerve blocking. Needless to say, this knowledge is not limited to anesthetists; however, the training and experience of the anesthesiologist does equip him with this knowledge more so than any other group of specialists, and other physicians should utilize this knowledge in attempting to relieve patients of pain or arriving at diagnoses.

Among intravenous agents available for relief of pain, procaine has outstanding value in treatment and alleviation of certain symptoms. It was first used intravenously during the recent World War to relieve pain during dressing of burns. Lundy was the first to use it for the pruritis of jaundice. On the basis of the reflex vasoconstriction, it has been reported helpful in treating post-traumatic edema and pain associated with fractures.[26] Its pain-relieving properties reduce the amount of morphine required postoperatively.[27]

Intravenous procaine is effective in the treatment of serum sickness,[28,29] although the exact mode of action is not known. Its use in the treatment of arthritic pain has been encouraging;[30] one infusion will relieve pain for varying periods up to two weeks or more. The usual technic is to dissolve 1 or 2 gm. of procaine hydrochloride in one liter of 5 per cent dextrose in water, or 5 per cent dextrose in saline, giving a 0.1 or 0.2 per cent concentration, and starting the venoclysis at a rate of about 60 drops a minute. If the flow is too rapid, the patient will experience certain sensations within five minutes. There is a warmth over the entire body, first noticed in the extremity receiving the venoclysis. The head and neck may be flushed, and there is a peculiar light-headedness or feeling of fullness and vascular congestion in the head. The flow should be slowed in the presence of these symptoms, as the patient can progress to convulsions and unconsciousness. Peterson and his coworkers[30] have given intravenous procaine to well over 2,000 patients with no case of procaine sensitivity or contraindication.

As a therapeutic agent, curare is limited principally to neuromuscular diseases.[31-33] It has been used in muscular rigidity of pyramidal tract and extrapyramidal tract origin.[32] Its use in poliomyelitis has been disappointing.[34] In some cases of spasticity it has increased the favorable results that were expected from orthopedic procedures and physiotherapy. Many cases of severe dysmenorrhea can be relieved by administering 50 to 100 units of curare intravenously.[35]

Although the use of curare in many of the above conditions has been reported, the results are not uniformly or consistently reliable, and one should not expect too much in such instances. The use of curare as a diagnostic test for myasthenia gravis is well established and its application to surgical anesthesia has been of paramount importance.

The use of oxygen inhalation is well established and the benefits generally recognized;[36] however, too often oxygen is withheld until cyanosis appears or as a last resort measure. Oxygen, like shock[4] therapy, should be started early before signs and symptoms of oxygen want appear. If the patient has any condition or operation which is likely to cause oxygen want, one is justified in initiating oxygen therapy. Such instances as postoperative transthoracic cases or many elderly patients with decreased vital capacity who have undergone moderately heavy surgery are likely candidates. One should be guided by the increased pulse rate as the earliest sign of oxygen want, or by central nervous system symptoms (nervousness, irritability, lack of cooperation, restlessness). Oxygen administered under positive pressure is more helpful for pulmonary edema than oxygen at atmospheric pressure. Helium-oxygen mixtures (80 per cent helium, 20 per cent oxygen) require less effort to breathe than air or oxygen alone, and are helpful to the asthmatic or dyspneic patient.

Treatment of postoperative atelectasis is the only one of the previously mentioned postoperative complications which has not been discussed. Early diagnosis is of utmost importance to prevent prolonged oxygen deficiency and its consequences. The lungs must be examined at least three times daily during the first seventy-two hours after operation. Tachycardia which cannot be explained otherwise is often due to minimal amounts of atelectasis. Physical changes in the lungs may be undetectable or minimal, but still capable of producing oxygen want and a rapid pulse. If one waits for fever, he has waited too long because secondary infection has started.

Under topical anesthesia of 2 per cent pontocaine hydrochloride, a straight urethral catheter, size 18F or 20F, is passed through the nose and into the trachea, by the blind technic or under direct vision. Moving it up and down in the trachea will produce violent coughing and the mucus is expectorated or can be suctioned through the same catheter. During this tracheobronchial aspiration the catheter is intermittently connected to the oxygen tank and the patient has oxygen delivered into the trachea at a flow or 3 to 6 liters per minute. It may be necessary to repeat the procedure two or three times, since the atelectasis may recur. This method is effective and eliminates the necessity of bronchoscopy in most cases.

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Electrocardiography in the Analysis of Clinical Problems

RAYMOND D. PRUITT*

MAYO CLINIC, ROCHESTER, MINNESOTA

Some months ago, an internist whose primary interest is in gastroenterology approached me looking a little confused and considerably annoyed. When, he wanted to know, were the cardiologists going to make up their minds on this matter of electrocardiographic leads. No more had he become familiar with the standard limb leads when the "fourth lead" came along. Just as confidence in his knowledge was returning, the fourth lead was replaced by multiple precordial leads. And now the confusion was made complete by the introduction of "V leads" and "unipolar extremity leads." I could understand his sense of frustration. I felt the same way about liver function tests.

One of the penalties of progress is the painful necessity of abandoning old and comfortable ideas for the strange and complex conceptions which investigative undertakings bring forth. Not that the new method is always the best method. Sometimes the only reward of study is the knowledge that the old way was preferable to the new. This sifting of ideas and technics is a tedious process and no one of us can hope to appraise accurately the developments within the full range of medical science. We must lean on each other.

It is my intention to review at this time the conclusions which my colleagues and I have derived concerning the value of certain developments within the field of electrocardiography. We would recognize that these conclusions are tentative, based on limited experience and subject to change with the acquisition of additional knowledge. But they represent the best we can do at this moment in time to sift the wheat from the chaff.

*Division of Medicine, Mayo Clinic, Rochester, Minnesota.

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THE SIGNIFICANCE OF THE PRECORDIAL ELECTROCARDIOGRAM

Precordial leads have been used in clinical electrocardiography for approximately fifteen years. In retrospect, three phases may be defined in the transition from the recording of the standard limb leads alone to the practice now prevailing in major laboratories throughout the Americas of taking from three to nine unipolar precordial leads. The first step was the recording of a single precordial lead in which the exploring electrode was placed on the thoracic wall at a point overlying the cardiac apex and the indifferent electrode was attached to one of the three extremities commonly used or to the back. This so-called fourth lead was subject to interpretation on the same empiric basis as the standard limb leads. In the minds of the majority, it was a "little more of the same."

The second step was the most significant if the least difficult of the three. It entailed only the simple process of moving the exploring electrode to several other points on the precordium, points overlying different portions of the cardiac surface. The significance of this advance was the recogni-

tion it accorded the basic fact that precordial leads are different from the limb leads. When applied to several points on the precordium the proximal electrode became in reality an exploring electrode, a means of determining the changes in electric potential produced by the heart beat in a relatively localized region of the myocardium. The interpretation of electrocardiograms recorded in this manner could be approached on the basis of certain simple concepts pertaining to the electric changes produced by tissues during the process of excitation. No longer was clinical electrocardiography bound to the empiric approach, fruitful and stimulating as that approach had been. The effects of injury, ischemia, hypertrophy and conduction disturbance could now be expressed in relatively simple terms, and an orderly arrangement of isolated facts began to evolve.

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THE third step in the evolution of precordial leads to their present status was the transition from CF, CR, and CL leads to the unipolar or so-called V leads. The difference among these several precordial leads is in the site chosen for the remote or indifferent electrode. When this latter electrode was placed on one of the extremities, it was removed a sufficient distance from the heart that the potential changes beneath it were of relatively slight magnitude as compared with those occurring at the exploring electrode. Though slight, these potential changes were of sufficient intensity to exert an influence on the form of the electrocardiogram.

As a means of achieving a more truly indifferent point of reference on which the remote electrode might be placed, Wilson and his associates[1] proposed the central terminal method. Making only those assumptions upon which the Einthoven triangle hypothesis is based, they showed that when lead wires from the right arm, left arm, and left leg are joined to a central terminal through appropriately placed resistances, the potential of that terminal will not be influenced by the heart beat. When the indifferent electrode of a precordial electrocardiogram is joined to this terminal, the deflection in the tracing will be an almost uncomplicated record of potential changes at the exploring electrode alone. Such a tracing may be described appropriately as a unipolar lead electrocardiogram. But even though they are more perfectly unipolar, the precordial leads obtained by the central terminal method are related very closely indeed to the imperfect unipolar precordial leads recorded when the remote or indifferent electrode was placed on one of the extremities. This can be readily demonstrated (Figure 1). Therefore all knowledge which was useful in the interpretation of CR, CL, and CF leads can be applied in the interpretation of V leads. The shift from one type of lead to the other does not constitute a revolutionary measure, does not necessitate abandoning established concepts and does not entail the adoption of a new approach. It is a slightly different and also a slightly better way of achieving the same old ends.

If the adoption of the central terminal method has significance, and I truly believe it has, that significance is not the relatively minor refinement which this technic affords over other methods of precordial leading. Rather, it is the recognition inherent in its adoption that those interested in electrocardiography have grasped the full significance of multiple precordial leads as a means of exploring the anterior surface of the heart. They have perceived the value of data derived from such leads in uniting knowledge gained by the experimental

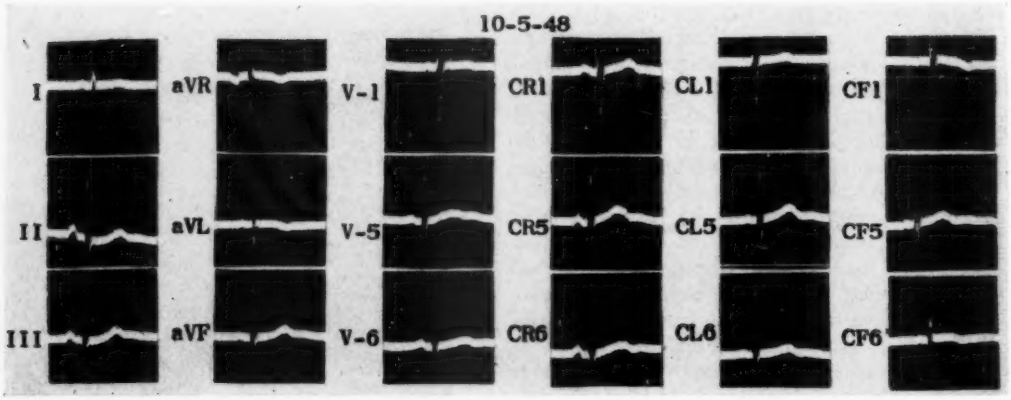

Figure 1. These electrocardiograms were taken on a healthy white man, 35 years of age. The heart occupies a vertical position from the electrocardiographic standpoint, the deflections in the unipolar lead from the left leg (AVF) resembling those in leads from the left side of the precordium (V_5 and V_6). Variations in the form of complexes in tracings made with the exploring electrode at the same point on the precordium (for example, V_6, CR_6, CL_6, and CF_6) are an expression of differences in potential changes at the indifferent electrode.

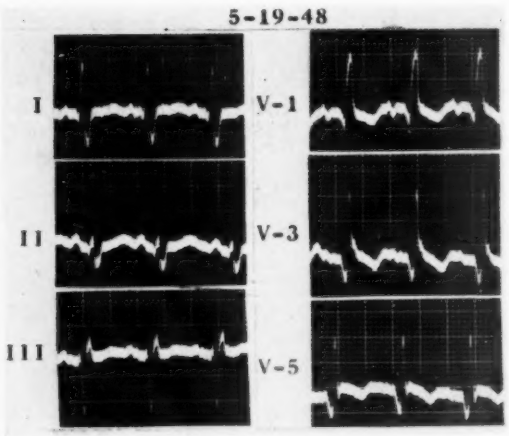

Figure 2. In the electrocardiogram are changes characteristic of right bundle-branch block. A lead from a point to the left of the transition zone was not recorded. However, the broad S wave in lead I and the final R deflection in V_1 are typical of right bundle-branch block. The Q wave in V_1 which increases in breadth and depth in positions further to the left is compatible with the presence of infarction in the anterior wall of the left ventricle.

approach with the facts obtained from clinical electrocardiography. In this union exists the basis for organizing our clinical knowledge around the well-established concepts of the dipole theory. Electrocardiography then becomes a science, albeit an imperfect one, whose problems are subject to solution by simple logic.

CERTAIN advances in electrocardiographic interpretation which have been a product of the use of multiple precordial leads are worthy of emphasis. These include:

1. The identification of right and left bundle-branch block. From an historical standpoint alone, the relationship of precordial leads to the problem of intraventricular conduction disturbances is both intimate and interesting. For it was in an attempt to secure exact data subject to ready interpretation that Wilson[2] and his associates, while studying the problem of bundle-branch block, introduced the multiple precordial leads into clinical electrocardiography. By use of these leads they were able to confirm other data supporting the conclusion that the views prevailing at that time concerning the identity of right and left bundle-branch block were incorrect.

2. The recognition of the electrocardiographic

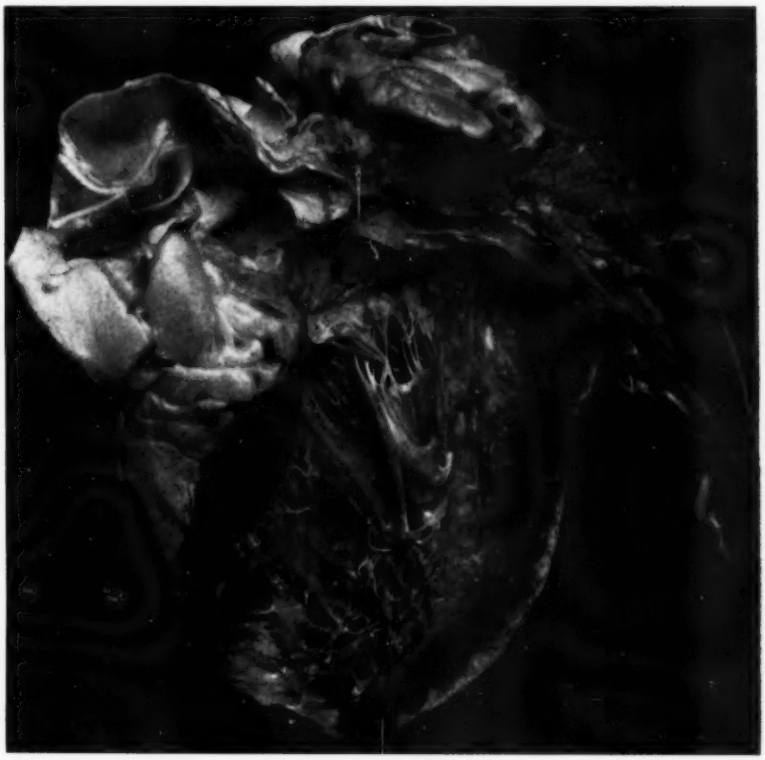

Figure 3. This specimen was obtained at necropsy from the patient whose electrocardiograms are reproduced in Figure 2. Scarring and thinning of the anterior and apical portions of the left ventricular wall secondary to myocardial infarction was present.

changes produced by myocardial infarction in the presence of right bundle-branch block. This relatively recent development is also a contribution of Wilson and his associates.[3,4] The correlation of theory, experiment and clinical data which formed the basis of this extension of our knowledge constitutes one of the most intriguing chapters in the evolution of the science of electrocardiography (Figures 2, 3 and 4).

3. The identification of anteroseptal infarction and relics thereof. This particular virtue of multiple precordial lead electrocardiography is the most convincing argument for the routine use of these leads in a practice made up in the main of patients in an age group where coronary sclerosis is common (Figure 5).

4. Clarification of the problem of ventricular hypertrophy has been achieved by application of concepts of the dipole theory in the interpretation of clinical records which included leads from points on the precordium overlying the surfaces of the right and left ventricles.

SIGNIFICANCE OF UNIPOLAR EXTREMITY LEADS

Because the potential of the central terminal is relatively unchanged by electric events associated with the heart beat, this terminal is the critical element in a method for the exploration of points on the body more remote from the heart than the precordium, sites at which potential changes are small compared with those commonly manifest on the precordium. The unipolar extremity leads represent an application of this possibility, VR being a lead in which the exploring electrode is placed on the right arm, VL on the left arm and VF on the left leg. In the development of certain concepts fundamental to an intimate understanding of electrocardiographic theory, these leads constitute an important element. My aim in this discussion.

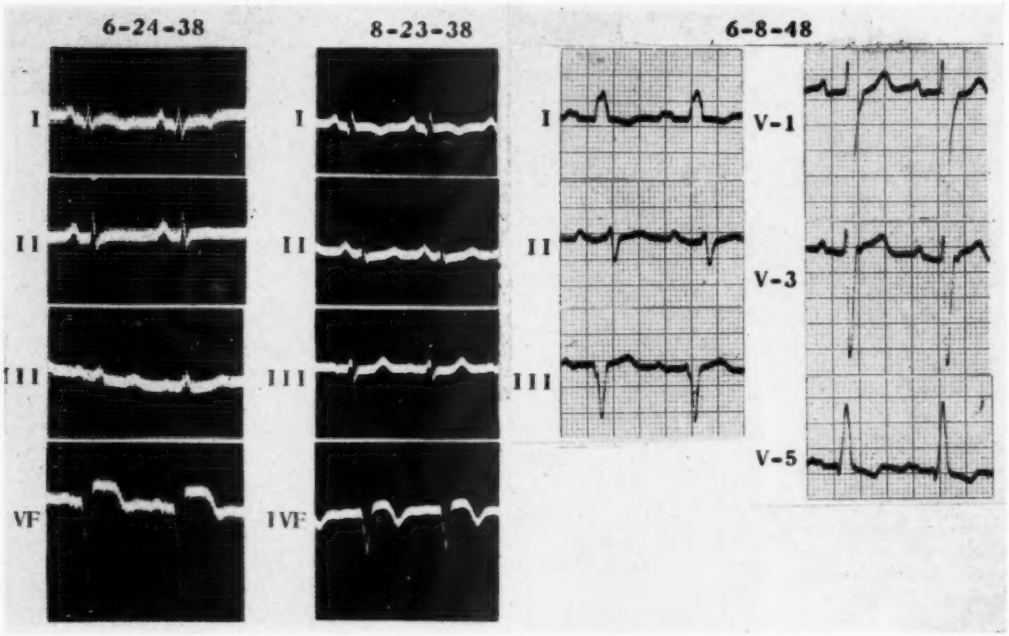

Figure 4. In the electrocardiogram recorded on June 24, 1938, changes characteristic of an acute anterior infarction are present. In the tracing of August 23, 1938, are seen changes associated with the healing stage of the same lesion. In the electrocardiogram of June 8, 1948, the complexes are typical of left bundle-branch block. With the possible exception of the small Q in V_5, there is no indication electrocardiographically of an old infarction. These findings are in keeping with the common experience that the incidence of left bundle-branch block obscures electrocardiographic relics of myocardial infarction.

however, is to assess their importance in clinical electrocardiography.

In essence, the unipolar extremity leads afford a means of making apparent facts which can be derived from the standard limb leads alone. In fact, the method for recording the unipolar extremity leads grew out of a study of the formulas for calculating the potential at a single extremity from data obtained in the bipolar standard limb leads.[5] With the central terminal method available it is expedient to take the extremity leads rather than make the calculations.

Use of the unipolar extremity leads has proved helpful in the study of three problems in particular; namely, (1) in the evaluation of the significance of the Q wave in lead III as an indication of posterior myocardial infarction, (2) in determining the electrocardiographic position of the heart, and (3) as a means of exploring portions of the heart inaccessible to precordial leads.

Now these are important problems and their study by means of unipolar extremity leads has produced knowledge of practical significance in clinical electrocardiography. Yet this knowledge can be used rewardingly in the interpretation of routine electrocardiograms in which the unipolar leads themselves have not been recorded.

In our laboratory, my colleagues and I take the unipolar extremity leads only in a few selected cases. Yet we apply the concept of the electrocardiographic position of the heart and the influence of position on standard limb and precordial leads over and over again. In a like manner, we recognize the importance of knowing that a Q wave in

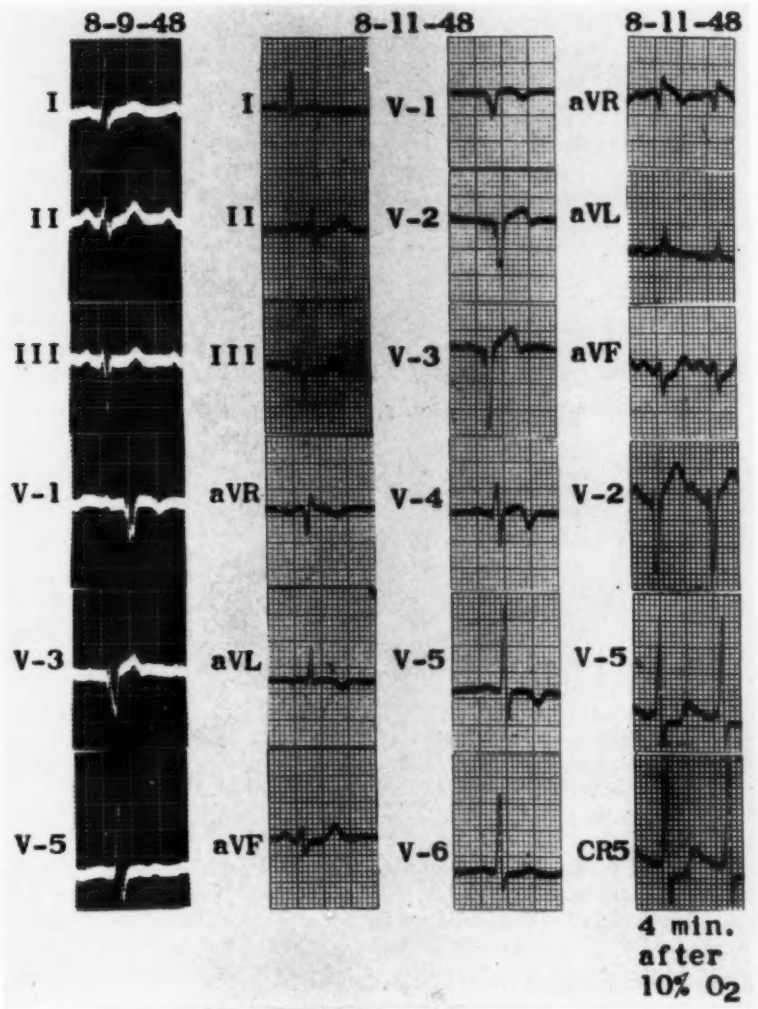

Figure 5. The patient was a 48-year-old man whose story afforded equivocal evidence of myocardial infarction. In the electrocardiogram of August 9, 1948, only the initial Q deflections in V_1 and V_3 afford any suggestion of myocardial infarction. The patient was sent for a full set of precordial leads and for an hypoxia test. The changes in the control tracings of August 11, 1948, are pathognomonic of anteroseptal infarction. After four minutes of hypoxia, marked segmental deviations appeared in leads AVR, AVL, V_5 and CR_5.

lead III is significant only inasmuch as it reflects early negativity of the left leg potential. The existence of such early negativity at the left leg is revealed most clearly in unipolar extremity lead VF. However, that negativity is indicated quite reliably also if a Q wave in lead III is attended by a Q II, an association the clinicial significance of which was and is recognized by clinicians unconcerned with the basis in theory for a correlation established by their experiences (Figures 6 and 7).

In summary, then, the unipolar extremity leads have found their greatest service in our hands in the teaching of electrocardiography. They afford a means of representing rather simply the solution to certain problems which had proved difficult heretofore. We think it would be ideal to take these leads routinely. However, the gains to be anticipated from such a practice in the solution of the

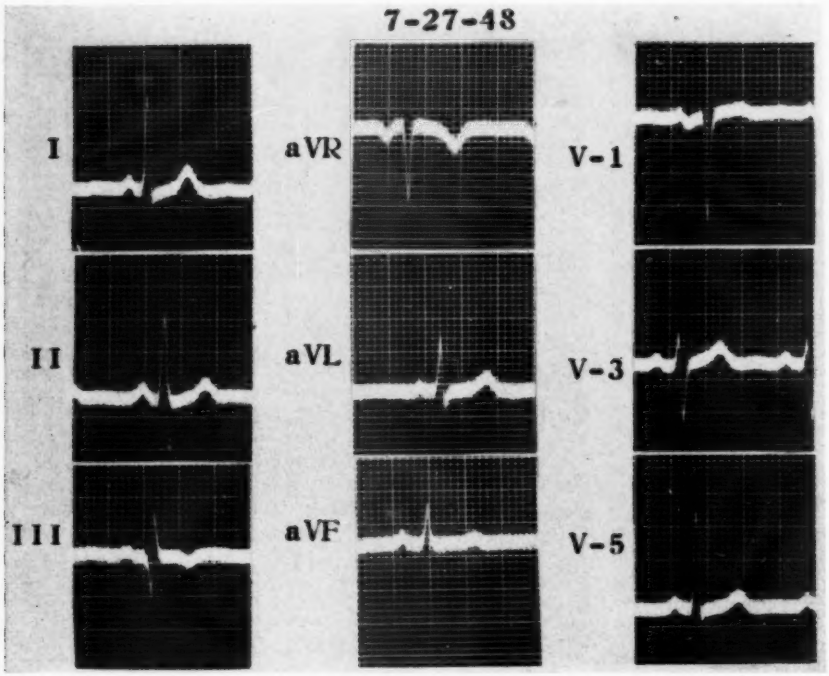

Figure 6. The patient was a white woman, 48 years of age, whose clinical examination afforded no evidence of coronary sclerosis or myocardial infarction. The electrocardiogram reveals a deep Q_3 and an inverted T_3. There is no Q wave in lead II nor in the unipolar lead from the left leg (AVF).

usual clinical problem appear limited. For practical reasons, we have restricted use of these leads to a comparatively few selected cases.

SIGNIFICANCE OF THE HYPOXIA AND RELATED TESTS

The final portion of this discussion will be devoted to the practical value of recording electrocardiograms on subjects who have been placed under some stress. In the diagnosis of coronary sclerosis, the need for a procedure more helpful than the routine electrocardiogram is felt acutely by all who are confronted by the vagaries in the manifestations of the disease. Since the symptoms of coronary sclerosis are more likely to be present when the heart is carrying an increased load, the electrocardiographic signs of the disease reasonably might be expected to appear more frequently under comparable circumstances. Such is the case. In certain patients electrocardiographic changes of a characteristic type do occur under conditions of increased stress, whether that stress be imposed by having the patient do physical work or by having him breathe air in which the oxygen tension has been reduced. Similar electrocardiographic changes may appear in tracings recorded during spontaneous episodes of angina pectoris.

In appraising the practical significance of these procedures, an answer must be given to four questions. First, in what percentage of patients who have coronary sclerosis with angina pectoris will characteristic electrocardiographic changes appear under conditions imposed by the test? The experience of several groups of investigators[6,7,8,9] provides fairly uniform data upon which an answer to this question may be based. About 50 per cent of patients in whom the diagnosis of angina pectoris can be established on other grounds will

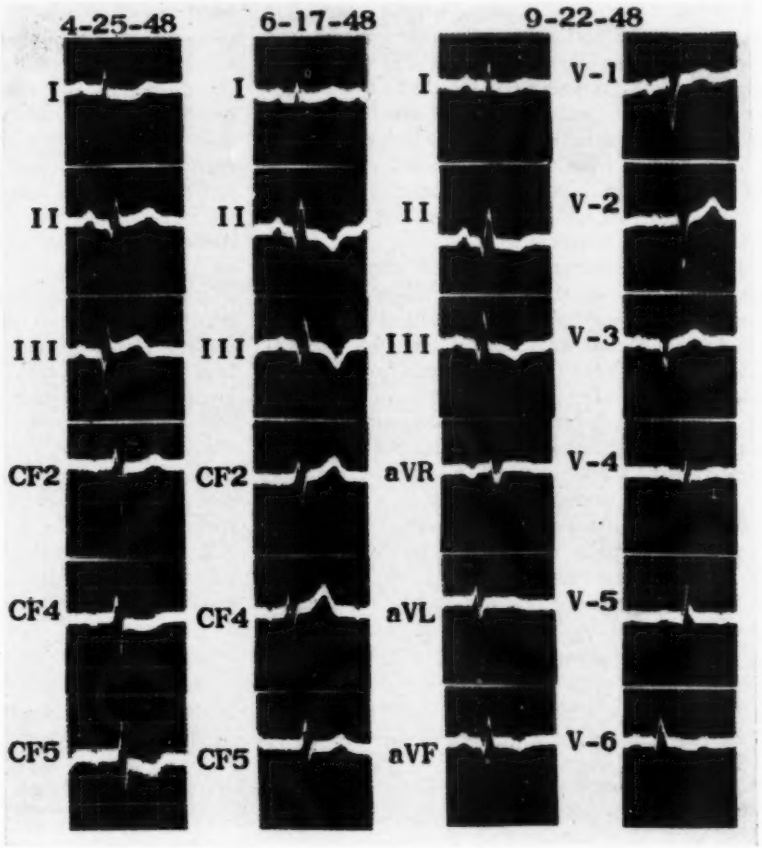

Figure 7.

These electrocardiograms were taken on a white man aged 57. In the tracings made on April 25, 1948, the changes are those of an acute myocardial infarction involving the posterior wall of the left ventricle. In the record of September 22, 1948, the Q waves in leads II and III and the unipolar lead from the left leg (AVF) represent relics of that lesion. It is of interest that there is also an abnormality in the development of the R wave in the precordial leads of September 22, 1948. The small R wave in V_1 is not associated with larger R waves in V_2 and V_3, but is replaced by a QS deflection in V_3. These findings are suggestive of scarring in the anteroseptal wall of the left ventricle. They may have been obscured in the earlier records where CF leads were recorded by the early negativity of the left leg potential.

have electrocardiographic changes characteristic of coronary insufficiency under the conditions imposed by the test. When the selection of patients is shifted to that group in whom there is some clinical evidence suggestive of angina pectoris, but evidence insufficient to establish that diagnosis, the test will give positive results in only about 1 out of 4. When the selection is extended to include a group of patients in whom the evidence of angina pectoris is even less convincing, the occurrence of a positive result becomes more infrequent.

Second, what is the significance of a negative result? Again agreement exists among several groups of workers that a negative result does not exclude the presence of clinically significant coronary disease. This fact is a corollary to the ob-

servation that among patients with a convincing story of angina pectoris, only 50 per cent will give a positive result. Therefore, procedures of this type do not fill the requirement for that most desired among tests: the means of excluding the presence of clinically significant coronary sclerosis.

Third, does a positive result afford reliable evidence of clinically significant coronary sclerosis? On the basis of our experience at the clinic, the answer to this question is "yes."

Fourth, is performance of the test attended by an appreciable risk to the patient? When conditions are properly supervised and patients carefully selected, the risk imposed by the procedure is minimal. We have encountered no fatalities and nothing more than transitory unfavorable reactions in the performance of more than 700 tests for diagnostic purposes.[10] This has not led to decreased respect for the load imposed by the procedure nor to reduced vigilance in maintaining safeguards for the patient undergoing the test.

Simple statement of these facts produces an impression more favorable than experience may justify of the importance of the hypoxia and related tests in clinical studies. From the standpoint of diagnosis, only when evidence pertaining to the state of the coronary circulation is of an equivocal nature does help from a procedure providing data of an objective sort attain paramount value. In such equivocal situations, however, the incidence of electrocardiographically positive results has been found to lie between 10 and 25 per cent. Consider, now, that performance of the test requires between thirty and forty-five minutes of time from a physician and a technical assistant and I believe it is understandable that there have been occasions after a run of seven or eight negative results when we have become quite discouraged in our efforts to obtain information by so tedious a process. But we have had other and more heartening experiences and these, I believe, will lead us to continued use of the test in a small percentage of our patients in whom the diagnosis of coronary insufficiency is an issue of major importance.

SUMMARY AND CONCLUSIONS

In the evolution of precordial lead electrocardiography, the major revisions have been required and accomplished in the field of attitudes and not of technics. It is the concept of a precordial lead as a means of exploring the anterior surface of the heart which is of importance. Whether this exploration is accomplished by V leads or by CR, CL, or CF leads is of far less significance than that the exploration be adequate. Conceptions of adequacy vary, but minimal requirements would appear to include leads from three points on the precordium, one of which should be to the right and one to the left of the transition zone.

The unipolar extremity leads find their major usefulness in the development of concepts basic in an understanding of electrocardiography. These concepts can be applied in the interpretation of standard limb leads and precordial lead electrocardiograms even though the unipolar extremity leads are not available. The routine taking of these leads appears desirable but not essential.

Even with the most refined technic and the most varied selection of leads, electrocardiography fails to supply evidence of the presence of coronary disease in many patients having symptoms which are related thereto.

A test which will exclude the presence of significant coronary disease remains on the list of desired but unavailable resources.

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Diagnostic Clinic

Lesions of the Breast

ARTHUR PURDY STOUT*

COLUMBIA UNIVERSITY COLLEGE OF PHYSICIANS AND SURGEONS, NEW YORK

Cancer of the breast is now first in frequency among all cancers. If detected and treated early by radical operation before lymph node metastases to the axilla have taken place, it is probable that 90 per cent of patients can be cured. Education of the public is bringing more women to their physicians for checkups on lumps in their breasts than ever before. Analysis shows, however, that 25 or more per cent of these women receive bad delaying advice from the first physician who is consulted.

There seem to be two important reasons for this. First, many physicians have never been taught the proper technic of breast examination, and second, they do not know how to interpret their findings in terms of therapy. I propose to devote most of the time at my disposal to demonstrating the technic of breast examination as we carry it out at the Presbyterian Hospital in New York. It has been developed in conjunction with my associate, Dr. Cushman D. Haagensen, and I believe that if carried out it will detect a great many suspicious lumps now missed. What you need for such an examination is an examining table, a chair, and most of all a gentle pair of hands. It is never necessary to be rough in the examination of the breast. Indeed, it is very bad to be rough, both because the massage of a cancer may possibly spread it, and, second, because you defeat your own purposes by being rough.

This colored patient, who has kindly consented to come here for examination, is 52 years old. Her mother died of old age and so far as she knows had no lesions of the breast. Nine years ago the patient had an operation for fibroids and has not menstruated since. She is married, but has never been pregnant. She has noticed a mass in the left breast for one year. Three months ago there was a bloody discharge from the nipple, and one month ago she noticed a sensation of heaviness or pain in the inframammary fold. She came to the hospital yesterday and so has had only her preliminary examination before coming here.

The examination of the breasts should include examination also of the axillae and supraclavicular fossae to determine the status of any lymph node enlargements in those regions. For the sake of convenience, we examine the supraclavicular fossae first because the patient is seated in a chair which is a good position for such examination. It is best to stand behind the patient, so that you can examine both sides and get in behind the clavicles and feel well down below. She has no supraclavicular enlargement. (Figure 1.)

Next we ask her to sit on the edge of the examining table. This is the first position for examination, with the patient sitting on the edge of the table and her feet on a chair. The examiner sits in front of the patient and slightly below her so that his eyes are about on a level with the nipples. We ask the patient to sit up straight and to keep her shoulders level. The first thing is inspection of the two breasts. One looks for asymmetry or any type of dimpling, edema, or any deformities of any sort. There is none to be seen in this position. If any were present they would be accentuated by asking the patient to put her hands on the top of her head.

Then we observe the nipples, projecting an imaginary line outward from them to see if that line makes an angle with the midline equal on both sides. If there is any lesion in one breast

*Professor of Surgery, Columbia University College of Physicians and Surgeons, New York, New York.

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ARTHUR PURDY STOUT

which is pulling upon the nipple so as to get it out of alignment, it at once becomes apparent in this position and one nipple line will be deviated in comparison with the opposite side. We refer to that as axial deviation of the nipple. It is not apparent in this woman. Of course, if there are congenital differences in the two breasts one has to inquire about them. (Figure 2.)

We next palpate the breasts, and here I would urge you to use the flat of the hand. It is never necessary to flex the fingers. Do not dig into the breast, but palpate it gently in this fashion. If there are masses you can feel them if they are close to the surface. It may not be possible to feel them in this erect position, but in the supine position which I shall ask her to assume in a moment it can be done. She has somewhat pendulous breasts, and in order to examine and feel them we can gently raise the breast up and move it around, thus looking for any dimplings or deformities which may be brought out by so doing. When I do that I can see a slight dimpling below and to the outer side of the left nipple in the areolar zone, and when one palpates in that region there is a small mass which can just be felt in this position.

I will not go through the examination of the other breast, but it is negative in this position.

Before she assumes the supine position we examine the axillae. The axilla can best be examined if the pectoralis major muscle is well relaxed. To do that, we ask the patient to let us hold her forearm; in this case it is her left forearm on my left forearm, so that I am supporting it and she is not. That will relax all the muscles around the axilla. (Figure 3.)

With the flat of the hand I insinuate my fingers as high into the axilla as possible and move the fingers up and down and then forward and backward. Anything in the axilla is then gently rolled over the underlying ribs. In this instance I can feel two small soft nodes, the larger of which I would say is slightly less than a centimeter in diameter. Similarly on the opposite side, I hold her right elbow and forearm on my right forearm and hand, and then insinuate my left hand as high up as I can in the axilla. When I do that, moving up and down and forward and backward, I can feel nodes of approximately the same size as on the left side.

Now we ask her to lie down on her back. For the examination of the left breast we ask her to raise the left arm above her head and roll toward the right side. A separate pillow or sandbag or, in this instance the same pillow, is tucked under the left shoulder so as to maintain this position without discomfort. The object of assuming this position is to spread the breast out over the chest wall as widely as possible. That enables one to have the least amount of tissue between the skin and the ribs and makes palpation of any nodules as simple as possible. Then with the flat of the hand again we palpate gently all over the breast. If the nodule is deeply seated and not easily felt, you will find that removing the source of visual impressions by closing your eyes while you palpate will enable you to direct your attention to what your fingers are feeling with a higher degree of concentration.

So I palpate all around, but the only thing that I can feel is a small mass in the position where I could feel it when she sat up, only now the mass feels larger. It is somewhat multinodular. It moves about very easily. The nodules have smooth surfaces, and although I can't demonstrate it to you, gentle pressure on this mass causes a drop of bloody fluid to come out at the nipple orifice from the corresponding nipple duct, so that we can feel

assured that the source of the discharge in this case is from this mass. (Figure 4.)

I again move the whole breast about (I always do it gently so as not to hurt her) and again I can demonstrate in so doing that at the site of the mass when the breast is raised up in that fashion there is a sinking in of the skin, which shows as a cup-shaped depression.

The examination of the other side is carried out in the same way, except that for the right side she rolls over part way on her left side and raises her right arm above her head. Then we palpate in the same way, and this breast is negative.

I have one more thing that I should like to demonstrate while the patient sits on the edge of the examining table with her feet on the chair. Frequently it is very desirable to find out whether or not a mass in the breast has any attachment to the pectoral sheath, because if it is a malignant lesion you want to know whether it is advancing toward the sheath or actually invading it. We ask her to put her hands on her hips and first observing the uninvolved side we ask her to press upon or to squeeze her hip. That serves to contract the pectoralis major muscle on that side, and if there is anything in the breast attached to its sheath, it will cause either a part of or the whole breast to be pulled upward.

Now we will do it on the opposite side. There is no difference between the two sides, and so we can feel assured that this mass just below and to the outer side of the left nipple is not attached to the pectoral sheath.

Figure 1. Examination of supraclavicular fossae.

If you will take the time (and you see that it has not taken me very long to go through the examination) you will be able to detect a great many lesions which you would fail to detect in any other way, and you will get information about the lump which you would fail to get in a more casual examination by simply asking the patient to expose the breast and then flexing the fingers and thumb like a claw—please forget that pincer motion!

This patient has a multinodular lump which has been present for a year and which has caused a bloody discharge from the nipple for three months. It is nodular, it has a smooth surface, but there is a cup-shaped dimple or depression produced over the lump when the breast is moved.

What is it? That brings us to the question of the bleeding nipple. In our experience bleeding from the nipple is very rarely an early sign of cancer of the breast. On the other hand, in about 85 per cent or more of patients with a discharge from the nipple which is non-lactational, the discharge comes from an intraductal papillary tumor which is benign, very commonly situated, as is this lump, in the areolar or nipple zone. However, since there is a dimple over this we cannot feel sure that it is not cancer, and so the indications here are that it should be explored with permission to do a radical operation if it should prove to be cancer. It should be biopsied and a quick frozen section done at the time of operation. If it proves to be cancer, the radical operation should be carried out. If it proves not to be cancer, the treatment that is recommended for these intraductal papillary growths near the nipple is to remove a pie-shaped piece of breast tissue with its apex in the nipple and its base going out for a distance into the surrounding mammary tissue. The reason for so doing is that these papillary growths are not always solitary but sometimes there is a group of them.

This case also permits me to call to your atten-

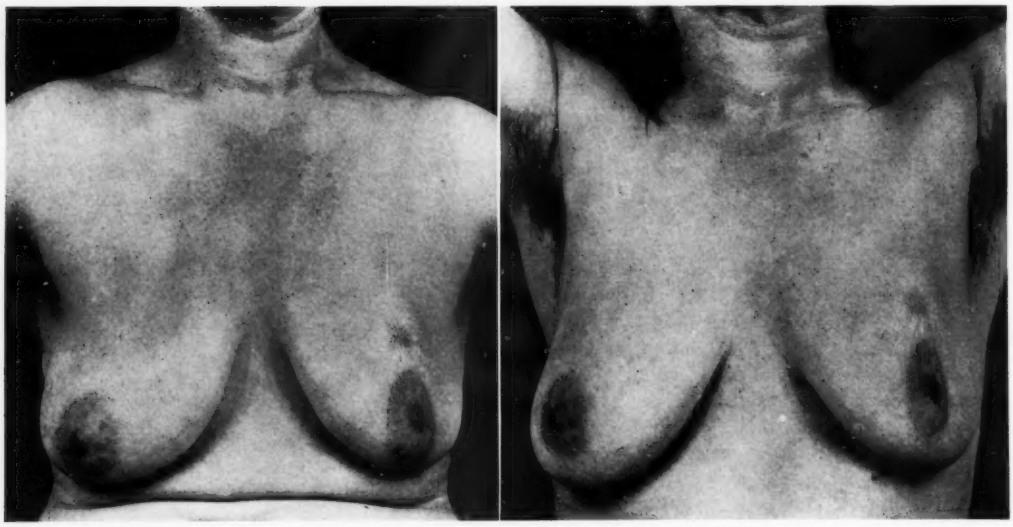

Figure 2*a* (left). Observation in the upright position, with arms down. 2*b* (right). Observation in upright position with arms elevated.

tion the handling of what we like to call the dominant lump in the breast. Many women have lumps in their breasts. If they are multiple and if they are more or less of the same consistency so that none is harder or different from any of the others, we feel safe in not exploring such a lesion. We can believe that it is chronic cystic disease and does not require treatment, only watching. But if the patient has a single lump in the breast which has a different consistency (generally it is harder) from any other lump in either breast, we use the term "dominant lump" for that.

Do not attempt by skill in clinical diagnosis to differentiate a cyst or a benign tumor from a cancer. You never can live long enough to get so experienced that you can tell all of them apart. The dominant lump must be explored to find out whether or not it is cancer, and that is particularly important in breast examination, in my opinion. Do not send the patient away saying, "That lump is nothing, it will do no harm." If it is a dominant lump it must be explored to determine its nature.

The treatment of cystic disease in our experience does not call for surgery unless a portion of the cystic disease forms a dominant lump. We are now engaged in an effort to find out whether or not cystic disease with or without epithelial hyperplasia is a pre-cancerous lesion. Many people will tell you that it is, and some have even urged a prophylactic mastectomy to prevent the woman from getting cancer. In our opinion that is not justified and we do not practice it. We are following these patients and trying to determine how many of them develop cancer, but it is a life-time job. You must follow them for the rest of their days, and it takes a very long time to determine it. The exact relationship of cystic disease to cancer is still undetermined.

Sometimes you find erosion of the nipple or an eczema-like inflammatory lesion involving the nipple and areola. Do not neglect that. It is your duty to find out whether or not it is Paget's disease of the nipple, which is a form of cancer that is spreading from either a demonstrable or an occult cancer hidden in the breast. If there is no mass in the breast that you can palpate, you should take a biopsy of the lesion of the nipple. It is very simple to find out by so doing whether or not it is cancer.

I have devoted my discussion principally to demonstrating the technic of examination and to the problem of what to do when you encounter a

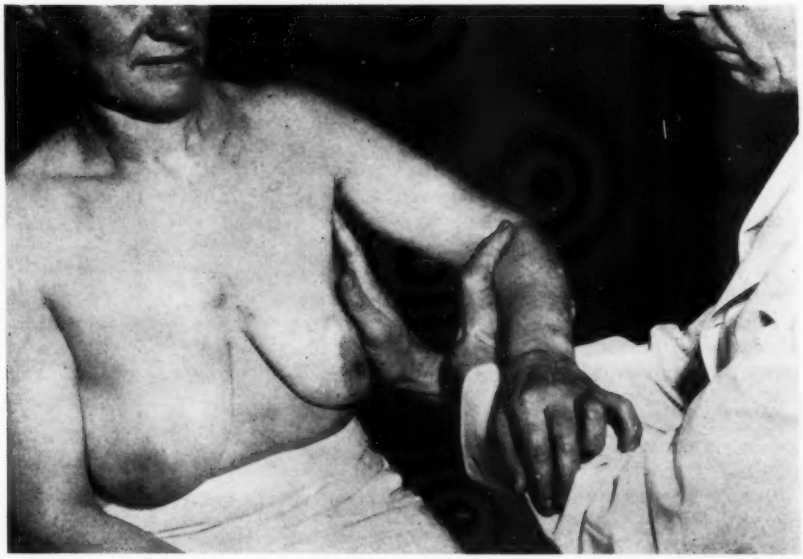

Figure 3. Examination of the axillae.

Figure 4. Examination of the breast with patient in supine position.

lesion which is not cancer or about which there is doubt. Let me simply say about cancer when it is discovered that in our opinion (I speak for Dr. Haagensen and myself) the cure of cancer is accomplished by radical mastectomy. It is uncertain as yet whether or not radiotherapy or any other means can cure cancer, but it has been demonstrated that the radical mastectomy can do so. In our opinion, if the case is operable that should be the treatment.

Let me, however, leave the word with you not to neglect the breast in your general physical examination of women. It is an important organ. You may save the woman's life by discovering an unsuspected lump in the breast, and if the woman comes to you and has a dominant lump in her breast, please do not send her away and say "Oh, that's nothing; don't pay any attention to it," but send her to a surgeon so that the lump may be dealt with by radical surgery if it is cancer or simply removed if it is a benign lesion.

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ABDOMINAL PALPATION

One of the major procedures for the diagnosis of abdominal pain available to every old-time physician was, as it still is in modern physical diagnosis, abdominal palpation. The skilled old-time physician in this reproduction of an old, familiar scene was Dr. R. T. Adams (1864-1935), who was a veteran general practitioner of Mantorville, Minnesota. (Reproduced by courtesy of the Mayo Foundation Museum of Hygiene and Medicine.)

Diagnostic Clinic

Surgical Aspects of Parkinson's Syndrome

W. JAMES GARDNER*

CLEVELAND CLINIC, CLEVELAND

PATIENTS with parkinsonism, or paralysis agitans, may be divided into three groups according to whether the condition is due to encephalitis, to arteriosclerosis, or is "idiopathic." The symptom complex, regardless of the causative factor, is strikingly similar in all cases, and is readily identified. The pathologic changes consist of cellular degeneration confined largely to the basal ganglia, particularly the globus pallidus and the substantia nigra.

Tremor and rigidity are the two outstanding symptoms; in occasional cases, one may occur without the other. The face is staring and expressionless, the head and trunk are usually inclined forward, and movements as a rule are slow, often seemingly very deliberate. In walking, the upper extremities do not swing as they do in the normal gait, but are carried rigidly in a characteristic semiflexed posture, with the hands in the "pill-roller" position. Tremor is most apt to affect the upper extremities, although it frequently also affects the lower extremities, the head, the tongue, and even the soft palate. The tremor is alternating, coarse, and rhythmic, occurs at the rate of 3 to 5 per second, is most pronounced when the extremity is at rest, and is apt to disappear with voluntary movement. The extremities are involved in a sort of plastic rigidity which lacks the springiness and resiliency of the spasticity accompanying a lesion of the pyramidal tract. The tendon reflexes are not usually altered and the Babinski response is absent. Blinking of the eyes is infrequent. The skin of the face, particularly in the post-encephalitic variety, is apt to be greasy, due to an excessive secretion of sebaceous material. Secretion of saliva is increased, especially in post-encephalitic cases, and the patient is apt to drool on his pillow at night.

Cog-wheel phenomenon is usually present. This can be demonstrated by passive flexion and extension of the forearm, accomplished in a step-like progression synchronous with the tremor. Speech is monotonous, sometimes slow, sometimes rapid, and often scarcely understandable. Ocular manifestations, such as impairment of convergence and accommodation, occasionally blepharospasm, and, in some instances, attacks of oculogyric crises, are common, particularly in the post-encephalitic variety. The oculogyric crisis manifests itself by a sudden upward rotation of the eyeballs so that the iris may be completely concealed beneath the upper lid. This position may be maintained for several minutes and occasionally even for hours, causing the patient great distress.

As the disease progresses, it becomes increasingly difficult for the patient to get up from a chair and to move about. Because of the rigidity of the neck and trunk muscles, he turns "all in one piece." A characteristic festination of gait may be exhibited; in this condition the patient leans forward and walks with increasing speed as he inclines still further forward as if hurrying to overtake his center of gravity. In other cases, the patient may suddenly be impelled to step backward, or to one side for several steps.

Difficulty in sleeping is common in these patients, and as the disease progresses, they become increasingly more disturbed, anxious, and depressed, but have no impairment of intellect. The tendency of the disorder is toward a steady progression, rapid in some instances, and very gradual in

*Department of Neurological Surgery, Cleveland Clinic, Cleveland, Ohio.

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W. JAMES GARDNER

others. Fluctuations in intensity of the symptoms occur as a result of emotional disturbances, physical illness or injury, and for no known reason. Altogether, this condition is one of the most distressing disorders to which the human flesh is heir.

The treatment of parkinsonism still remains essentially that of medical management. The drugs usually employed are atropine, hyoscine, or stramonium, and extract of belladonna root. More recently benzedrine and benadryl have been employed, and the newest drug to be used is myanesin. Because these drugs are effective only during the period of their administration and sometimes rapidly lose their effectiveness, surgical measures for the control of the symptoms have been proposed at various times.

Neurologists are not agreed as to whether the symptoms of parkinsonism are due to irritation of nervous pathways or represent a release phenomenon due to interruption of normal inhibition. It has been observed, however, that the tremor and rigidity of Parkinson's syndrome are relieved in extremities which have become paralyzed by a stroke. This observation, plus the fact that in some subjects the tremor of a limb may be more disabling than paralysis would be, has led the surgeon to seek to relieve the condition by cutting various nervous pathways.

Thus far, three areas in the central nervous system have been surgically attacked with some measure of success in an effort to control the rigidity and tremor of paralysis agitans. These areas are the spinal cord, the precentral cerebral cortex, and the basal ganglia. Since the location of the disease process itself appears quite inaccessible, and since the mechanism of the production of the tremor and rigidity has never been adequately explained, the efforts of surgeons in these instances have been directed toward interrupting the nervous pathway over which the tremor is transmitted. Furthermore, if the tremor and rigidity represent a release phenomenon, and not a direct result of irritation, it is unlikely that excision of the diseased areas of the brain, even if feasible, could produce relief.

The meeting of the Association for Research in Nervous and Mental Disease in 1940 was devoted to a consideration of diseases of the basal ganglia, and reports on surgical treatment were presented by Bucy,[1] Klemme,[2] Meyers[3] and Putnam.[4] Bucy observed relief of a mild unilateral left choreoathetosis in a child following excision of the right precentral gyrus. On reviewing the literature, he discovered that this was not a new observation, since Horsley, as early as 1890, had reported the relief of involuntary movements following excision of the precentral gyrus.

Bucy found that in 7 cases where involuntary movements were limited to, or predominantly involved, the extremities of one side of the body, the operation gave persistent relief in varying degrees. As a result of these observations he concluded that this area contains the neural mechanism which conducts from the brain to the spinal cord the impulses responsible for the involuntary movements. He found that wide excisions of the cortex in this area gave the most effective results, and that even extensive extirpations are consistent with the return of a remarkable degree of voluntary power in the involved extremity. When carried out on the dominant hemisphere, excision of the arm area results in a temporary expressive aphasia, which soon disappears. The operation may be followed by the development of convulsions.

At this same meeting, Klemme reported on the

treatment of parkinsonism by excision of the premotor cortex.[2] His report was most encouraging, although not very detailed. In a series of 100 cases there were 17 postoperative deaths and 6 complete failures. He did not describe the unfavorable sequelae, such as paralysis and epilepsy. Although this operative procedure was among the first to be employed in this condition, it has not been generally accepted by neurological surgeons because of the accompanying morbidity.

An alternative to cortical extirpation in the treatment of alternating tremor is sectioning of the lateral pyramidal tract in the cervical region, as proposed by Putnam.[4] He demonstrated that a complete section of the lateral pyramidal tract at the level of the second cervical vertebra curiously enough does not cause complete hemiplegia. As a matter of fact, after the initial paralysis, there is considerable return of voluntary power in the involved extremities. Putnam found that this operation apparently disturbs the function of the hand less than any of the operations upon the electrically excitable cortex. For this reason, and because it spares the speech center, he believes it is preferable for patients suffering from tremor of the right hand. Also, if both arm and leg or the leg alone is involved, pyramidotomy is probably easier and more conservative than the corresponding cortical operation.

In this procedure, the lamina of the second cervical vertebra is removed on the side of the proposed incision, which, of course, is the side of the severest symptoms. The dura is opened and the spinal cord exposed. With a pointed knife, the lateral columns are incised to a depth of 4 mm. The segment of the cord incised is that portion which lies between the line of emergence of the posterior roots and the attachment of the dentate ligament.

The results of spinal pyramidotomy in 22 cases of Parkinson's syndrome have been evaluated by Putnam.[5] These patients were all followed for more than twelve months after the operation. He found that of the various symptoms only the alternating tremor could be favorably influenced. In one-third of the patients, the tremor disappeared; in another third, it was satisfactorily diminished; in the remainder, the result must be considered as failure. Reduction of motor power occurred in all cases immediately after operation, but substantial recovery occurred in the majority of cases. Putnam believes that the disability appears to be less than that which usually follows cortical or subcortical operations for the relief of tremor. While this operation produces its best results in young individuals who suffer chiefly from severe alternating tremor, it often affords some comfort and relief in more severe cases with rigidity and other manifestations.

The problem of surgical therapy in parkinsonism, according to Meyers, consists of interrupting the nervous impulses responsible for the symptoms.[3] Ideally, this interruption should entail no damage to those structures upon the integrity of which depend the functions of motion, sensation, coordination, and intellect. After observing the effects of various types of operations upon the basal ganglions, Meyers decided that interruption of nervous pathways leading from the globus pallidus appeared to be the most effective in relieving the symptoms of parkinsonism, and, furthermore, it did not result in impaired function. He refers to this operation as interruption of the pallidofugal fibers. Meyers found that, following this operation, the alternating tremors were abolished or were rendered barely perceptible, and rigidity was effectually reduced with a consequent prompt improvement in the symptoms caused by it.

In his hands, it proved to be a relatively simple technical procedure. In this operation, a craniotomy is performed at the anterior vertex on the side opposite the most severe symptoms. The anterior horn of the ventricle is entered through a cortical incision. The head of the caudate nucleus and the foramen of Monro are exposed. An incision is made through the fiber tracts leaving the globus pallidus in the region of the foramen of Monro. At the time of his last report, Meyers was of the opinion that this operation could be applied to bilateral as well as unilateral cases of paralysis agitans, although he had not as yet employed it on both sides.

Jefferson Browder[6] favors what he terms the capsular operation for parkinsonism. In this operation, the dorsal half of the head of the caudate nucleus is first removed, and then the fibers of the anterior limb of the internal capsule are divided up to within a few millimeters of the knee of the internal capsule. Browder feels that this operation should be carried out only on one side, and it is employed, therefore, only in cases in which the manifestations of the disease are predominantly on one side. He performs the operation under novocaine anesthesia without preoperative medication.

A craniotomy is performed to expose the falx and upper frontal region in front of the premotor area on the side opposite the tremor. An incision is made in the cortex and carried into the anterior horn of the ventricle to expose the head of the caudate nucleus.

The upper, or dorsal half, of the structure is removed in order to expose the inner fibers of the anterior limb of the internal capsule. With a blunt, right angle hook, the surgeon then gradually divides the fibers of the anterior limb of the internal capsule a few at a time until the tremor is abolished and a very marked weakness of the hand is produced. Postoperatively, the patient exhibits a pronounced hemiparesis, which begins to clear in about ten days, but does not disappear entirely.

Browder employed this procedure in 15 patients with parkinsonism, 9 of whom had as the outstanding symptom gross, alternating tremor, limited for the most part to the extremities of one side. The tremor was abolished in 6, absent for the most part in one, and diminished for six to eight weeks in 2. In 6 cases of bilateral involvement the results of the unilateral operation were poor. Three patients died, and although tremor in the remaining 3 was relieved on one side, the situation as a whole was not improved. Three patients have survived the operation for five years without recurrence of the tremor. One of these has had four generalized convulsions in that time, but they have not interfered with his employment as a watch repairman.

Browder stresses the fact that parkinsonism cannot be cured by surgical therapy; improvement following operation is nothing more than symptomatic relief. The surgery performed has merely interrupted an arc of abnormal neural mechanism, and has in no manner altered the underlying pathologic process; however, it is his opinion that, in properly selected patients, surgical therapy offers more in palliation than any other method available at the present time. By properly selected patients, Browder refers to relatively young adults with incapacitating unilateral tremor, or in whom there has developed a psychologic reaction that has caused them to withdraw from society.

Another method of surgical approach to this problem was suggested by Risteen and Volpitto.[7] They noted in carrying out stellate ganglion blocks in cases of hemiplegia due to vascular accident that there was a reduction in the degree of spasticity. The rationale behind this mode of therapy was interruption of vasoconstrictor impulses to the brain. Their experience with relief of spasticity in patients who had had a stroke led them to try the procedure in cases of parkinsonism. They observed that with repeated stellate ganglion injections, extrapyramidal rigidity diminished, but the tremor was not essentially altered.

We have been able to confirm the observations of Risteen and Volpitto that the relief of muscular rigidity in paralysis agitans may be affected, temporarily at least, by novocaine block of the cervical sympathetic chain. This effect may be due to increased blood flow through the brain.

In a series of 34 cases of Parkinson's syndrome, therefore, we attempted to make permanent the relief afforded by cervical sympathetic novocaine block by surgically interrupting the sympathetic nerves supplying the cerebral blood vessels. It was found that the most effective interruption was accomplished by excision of the superior cervical sympathetic ganglion. The operation, in each case, was carried out on both sides.

In this series of 34 cases, 21 were the result of a previous attack of encephalitis, 10 were due to arteriosclerosis, and 3 were of the so-called idiopathic variety. In selecting the cases, those having rigidity as the predominating symptom were chosen. The ages varied between 37 and 69 years, the average age being 53.8 years. Patients in all stages of the disorder were selected, with signs and symptoms ranging from minimal to far advanced. There were 2 postoperative deaths, both of them in far advanced bilateral disease.

These cases were studied from six to twenty months following operation. The most significant improvement noted was an alteration of mood. In 20 patients, the emotional tone was improved. A number of these patients were pleased, or even enthusiastic, about the results of the operation, although the examiner in most of these instances was unable to demonstrate objective improvement. Some improvement in the rigidity was noticed in 14 instances, with pronounced relief in 4 cases. The lessening of rigidity in these cases may be attributed to increased animation, the result of improvement in mood. As is the case with other conditions treated by sympathectomy, the degree of improvement present immediately after operation may not be maintained.

The tremor of Parkinson's syndrome is not altered by interruption of the sympathetic nerve supply

to the brain. Four patients in this series claim some improvement; none had complete relief. Two patients felt that there was some increase in the amount of tremor, and 3 had oculogyric crises as concomitants of their Parkinson's syndrome. Of this number, none had complete relief, but one observed some reduction in the number of the attacks. Other symptoms, such as disturbance in sleep rhythm and increased salivation, were not affected by the operation.

THE ill effects of the operation are as follows: In 21 cases, approximately two-thirds, the patients experienced a fleeting, sharp pain in the region of the parotid glands upon taking the first bite of food. Pharmacologic tests indicate that this is apparently due to the fact that the parasympathetic vasodilator impulses to the parotid glands are no longer inhibited by sympathetic vasoconstrictor impulses, so that there occurs following the gustatory excitation a sudden, brief vasodilation, causing tension in the capsule of the gland, with the resulting fleeting pain. This symptom can be benefited by light doses of x-ray therapy to the parotid gland. Sixteen patients complained of varying degrees of nasal stuffiness postoperatively, due to engorgement of the nasal mucosa. This was annoying only when the patient was in the horizontal position. It is particularly apt to occur in allergic individuals, and can be controlled by the use of vasoconstrictor nose drops. Transient hoarseness due to vocal cord palsy occurred in 6 cases postoperatively, but in one case has persisted for several months. Four patients reported that their condition was aggravated by the operative procedure, although examination did not indicate any degree of advancement except that which might be expected by the natural progression of the disease. Most of the patients in this series, in response to a direct query, indicated that they felt the operation was worthwhile.

It is our present feeling that cerebral sympathectomy, accomplished by resection of the superior cervical sympathetic ganglia, is of slight value in the treatment of Parkinson's syndrome. The chief benefit is a favorable alteration of the mood, and this may be responsible for reduction of rigidity and improved ability to perform physical acts in a few instances. The procedure can be applied to bilateral cases where rigidity rather than tremor is the chief complaint, and in the age group where more radical surgery is contraindicated.

In conclusion, it may be stated that none of the present-day operative procedures is entirely satisfactory. However, the distress of these patients, the relative ineffectiveness of medical treatment, and the occasional brilliant surgical results continue to stimulate efforts in this field.

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UNIVERSITY OF WISCONSIN TO BROADCAST MEDICAL LECTURES

RADIO is being put to practical use for postgraduate medical education by the University of Wisconsin Medical School at Madison in a project designed to aid the medical practitioners of the state. The school has arranged to use the frequency modulation facilities of the university's radio station to broadcast medical conferences, symposiums and lectures of interest to the practitioner. The county medical societies will cooperate in arranging for local reception of the broadcast, which will be scheduled from time to time as such programs take place.

Diagnostic Clinic

Extreme Insufficiency of the Anterior Lobe of the Pituitary Gland

RAY F. FARQUHARSON*

UNIVERSITY OF TORONTO FACULTY OF MEDICINE, TORONTO, ONTARIO

SIMMONDS' disease, extreme insufficiency of the anterior lobe of the pituitary gland, is a characteristic syndrome which follows various destructive pituitary lesions. The most common cause is necrosis of the gland which may occur in the puerperium if the patient suffers severe collapse from hemorrhage; the anterior lobe, greatly enlarged during pregnancy and beginning to involute, is then peculiarly susceptible to thrombosis which may occur as a result of the circulatory stasis associated with hemorrhage, collapse, and prolonged fall in blood pressure.

The syndrome may also be caused by fibrosis, either spontaneous or following gumma or trauma and hemorrhage. Relatively few cases are due to intrasellar tumors even when the tumors are large enough to dilate the sella and interfere with neighboring structures, because sufficient glandular tissue is left to prevent the development of marked insufficiency.

It is important to point out that symptoms of pituitary insufficiency do not appear until approximately two-thirds of the anterior lobe has been destroyed. Accordingly, lesions such as the relatively common chromophobe adenomas may be found in patients who have had no significant change in endocrine function. The first manifestations of insufficiency are those of secondary sexual failure—amenorrhea in women, impotency in men, or sterility with loss of secondary sexual characteristics in both. Patients presenting symptoms of marked sexual insufficiency are always weak and tired; with more destructive lesions these general symptoms become more severe. Not until about 90 per cent of the anterior lobe has been destroyed, however, does the full syndrome appear with secondary atrophy and loss of function of the thyroid and adrenal glands and general impairment of vital functions.

Such patients become chronic invalids who feel the cold intensely and are dull, apathetic creatures, weak and tired both mentally and physically. They are thin, pale, wrinkled and old in appearance. Axillary, pubic, and body hair have all disappeared. There is a normochromic anemia but, partly because of decreased pigmentation, the pallor of the skin is out of proportion to the anemia. One finds low fasting blood sugar, low basal metabolic rate, low temperature, pulse, and blood pressure. There may be coma and convulsions caused by hypoglycemia or crises of adrenocortical insufficiency. On examination, one is struck by the wizened, aged appearance, the loss of body hair, and the atrophy of breasts and genital organs.

Before discussing the diagnosis of individual cases, it should be emphasized that lesions limited to the pituitary gland do not cause obesity. Obesity does follow upon hypothalamic injury, and some lesions, such as tumors, may damage both the pituitary gland and the hypothalamus and give rise to a syndrome of obesity and gonadal hypofunction which has often been referred to as Fröhlich's syndrome or adiposogenital dystrophy.

CASE REPORTS

Case 1—Mrs. S. S. had been a healthy, active person weighing about 140 pounds (height, 65 inches) until the birth of her fourth and last child some twelve years before her death in 1935 at the age of 45 years. The

*Department of Medicine, University of Toronto, and the Medical Service, Toronto General Hospital, Toronto, Ontario, Canada.

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Figure 1 (Case 1). *Left,* photograph taken in 1923 shortly before the birth of her fourth and last child. Weight 140 pounds; height 65 inches. *Right,* 1931, when the patient weighed 85½ pounds.

(Figures 1, 2, and 3 from: Farquharson, R. F.: Simmonds' Disease—Extreme Insufficiency of the Adenohypophysis, to be published by Charles C Thomas, Springfield, Illinois.)

birth was followed by puerperal fever (history of hemorrhage not obtained), and she was never well again. Menses never recurred, all axillary and pubic hair fell out, and she became extremely weak and tired. She lost weight until she was quite emaciated. She complained of the cold even in the summer months. A gradual mental deterioration took place; she became dull, careless of her person, resentful of interference, and difficult to live with. In 1931 she became unconscious, with fever, and was admitted to the Toronto General Hospital.

Her weight on admission was 85½ pounds, and she looked old and small. There was no axillary, pubic, or body hair; the skin had little pigment, the pallor being out of proportion to the moderate anemia (hemoglobin 50 per cent). The breasts and genital organs were atrophic. Her basal metabolic rate was −30 per cent. She had a low fasting blood sugar, varying usually between 40 and 60 mg. per 100 cc. The blood pressure was low and an electrocardiogram showed low voltage.

Solutions of dextrose in saline were administered and she improved slowly. After administration of thyroid, her basal metabolic rate rose to −3 per cent, with little clinical improvement. During several subsequent weeks in the hospital she cooperated badly, and she finally refused further treatment and returned home where she was dirty, negativistic, and careless of her person.

Late in 1931 she began to improve spontaneously; she slowly gained in weight to about 110 pounds and began to take some interest in her surroundings. The amenorrhea persisted, however, and she remained mentally dull, weak, tired, and sensitive to cold.

In 1935 she was brought to the hospital in coma from a crisis of adrenocortical insufficiency. Her temperature was 106° F., pulse 120, and blood sugar 48 mg. per 100 cc. She died two hours after admission.

An autopsy disclosed the destructive lesion of the anterior lobe which is typical of puerperal necrosis: almost all of the lobe had been destroyed; only a small

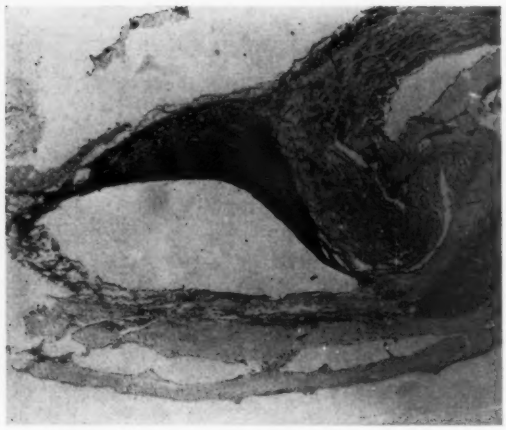

Figure 2. Microphotograph of the pituitary gland in Case 1. It shows the typical late lesion of puerperal necrosis. The posterior lobe is intact but the anterior lobe is largely destroyed and is represented only by a small triangular remnant of shrunken cells in the superior angle just in front of the stalk. There is no fibrosis.

Figure 3. Microphotograph of the pituitary gland in Case 2. There is virtually complete destruction of the whole gland, a few glandular cells persisting here and there in the coarse fibrous connective tissue which is infiltrated with lymphocytes.

fragment of shrunken, atypical cells was found; the posterior lobe was intact. There was marked secondary atrophy of the ovaries, thyroid, and adrenal glands and a general microsplanchnia.

The diagnosis in this case was obvious because of the onset of gonadal insufficiency immediately after an abnormal puerperium and the early development of the typical severe syndrome. The attacks of coma with fever and low blood sugar due to adrenocortical insufficiency occur only in severe cases and are a common cause of death.

A matter of great interest was the spontaneous gain in weight and improvement in general condition after she had refused further therapy. It is to be noted also that, like many patients with Simmonds' disease, she showed little improvement on thyroid therapy. Actually these patients are very sensitive to administration of thyroid, which may lead to crises of adrenocortical insufficiency. Administration of thyroid should be begun only after treatment of the adrenocortical insufficiency has been successfully undertaken, and the initial dosage should be small—¼ to ½ gr. per day, increased after several months only if symptoms of hypothyroidism persist after initial improvement.

Case 2—W. D., aged 50 years at death in 1931, had been in good health, weighing about 160 pounds (height, 71 inches), until two and one-half years before death, when he rapidly gained in weight to 185 pounds and lost sexual desire. One year before his death he began to lose his sense of well-being and became tired, weak, and pale. His appetite failed and he lost weight. About nine months before death, he complained of epigastric distress and vomiting one-half to one hour after eating, but these symptoms soon disappeared. Then a great change in personality occurred gradually; he showed at first gross emotional disturbances, then apathy, lethargy, and finally vegetation.

Six months before death he weighed 125 pounds; two months before death, 108 pounds. He looked wrinkled, old and small; his skin was pale, with little pigment. There was no axillary, pubic, or body hair and little hair on his face. Temperature, pulse and blood pressure were low. His basal metabolic rate was −35 per cent; it rose, with very slight clinical improvement, on thyroid therapy. His fasting blood sugar varied between 25 and 70 mg. per 100 cc., and he was very sensitive to small doses of insulin. Treatment with thyroid and anterior pituitary extracts failed to help his condition.

This man presented the typical picture of severe anterior pituitary insufficiency. The early gain in weight associated with loss of sexual desire suggested the presence of a lesion with hypothalamic disturbance. The finding of a strongly positive Wassermann reaction in blood and spinal fluid offered a reasonable explanation (he had gonorrhea in early life); it was assumed that a large gumma of the pituitary gland had given rise to a hypothalamic gain in weight some two and one-half years before death and then progressed to fibrosis.

At autopsy in 1931, the entire pituitary gland was extremely shrunken, the few remaining glandular cells

being interspersed in the masses of fibrous tissue which was infiltrated with lymphocytes.

Case 3—Mrs. D. S., aged 51 years, was seen a few weeks ago and has not yet come to the hospital for full investigation and treatment. She had been a healthy person until the birth of the last of her 10 children in 1935, when she had a puerperal hemorrhage. She was unable to nurse the infant, although she had nursed all her other children without difficulty. She noticed immediate disappearance of all pubic and axillary hair; she never menstruated again nor did she have further sexual desire. Her weight fell gradually from 135 to 113 pounds but, having a height of only 58½ inches, she was not thin. She has been tired and weak and slightly sensitive to cold ever since but has been able to do her housework with difficulty and care for a sick husband.

She is a pale, moderately well-nourished woman with no axillary, pubic, or body hair. Her breasts are atrophied and there is stenosis of the vagina. Pulse and temperature are normal; blood pressure 115/74 to 90/64; basal metabolic rate −20 per cent.

This patient presents a picture of mild insufficiency of the anterior lobe of the pituitary gland. There is no reasonable doubt that she suffered necrosis of perhaps three-fourths of the anterior lobe at the time of the puerperal hemorrhage thirteen years ago but she is able to carry on because sufficient glandular tissue remains to prevent gross functional failure of the thyroid and adrenal glands. It is possible that she will be helped by the administration of chorionic gonadotropin, 500 units three times a week.

Case 4—J. M., 54 years of age, and the father of 3 children, was well until ten years ago when he began to complain of failing vision. He was examined at that time and found to have a bitemporal hemianopia and an enlarged sella turcica. He refused treatment and continued to work as a caretaker.

In recent years he has been rather sensitive to cold and has lost sexual desire. He is pale and lethargic with gross defects in memory, and is confused and stuporous at times. Axillary and body hair are absent; facial and pubic hair sparse. Gonads and penis are not atrophic but the prostate gland is very small. There are no notable changes in temperature, pulse, blood pressure, blood sugar or blood hemoglobin. He has not been able to cooperate well enough for measurement of basal metabolic rate. Radiologic examinations reveal a greatly enlarged sella with a huge tumor extending up between and bulging into one of the lateral ventricles.

He appears to suffer from a chromophobe adenoma with hypogonadism secondary to pituitary insufficiency. As in so many tumor cases, sufficient glandular tissue remains to prevent the development of the syndrome of Simmonds' disease.

These four patients present different types and degrees of insufficiency of the adenohypophysis. It is apparent that Simmonds' disease is not an entity but a condition of almost complete insufficiency of the anterior lobe, which may be caused by a variety of destructive lesions of which the commonest is necrosis occurring at the time of a puerperal hemorrhage. There is no predisposing, constitutional type of person. The onset varies with the extent and rapidity of development of the destructive lesions; it may be immediate and abrupt as in severe cases of extensive puerperal necrosis, or gradual as in instances of tumor and granuloma. Even in cases of puerperal necrosis the onset may sometimes be delayed for years till a remaining fragment undergoes further atrophy or degeneration. The final clinical picture is, however, the same in all types if the destruction of the gland is virtually complete.

One might well point out that Simmonds' disease rarely leads to the severe degree of emaciation noted in the first two cases. In two other patients with Simmonds' disease, treated at the Toronto General Hospital and examined at autopsy, there was no emaciation.* In general there is loss of weight leading to thinness but seldom the emaciation seen in common wasting diseases or in anorexia nervosa. The average weight of 22 uncomplicated proved reported cases of Simmonds' disease caused by puerperal necrosis was 105 pounds.

DIAGNOSIS

The diagnosis of Simmonds' disease is easily made if the condition is kept in mind and the onset of endocrine symptoms dates from a complicated puerperium or is associated with gradually increasing signs of an expanding lesion in the sella turcica. All severe cases, whatever their etiology, are easily recognized by the presence of severe gonadal insufficiency with loss of secondary sexual characteristics and the development of extreme weakness and fatigue with manifestations of insufficiency of thyroid and adrenal glands and late mental changes.

The conditions most commonly confused with Simmonds' disease are adrenocortical insufficiency, hypothyroidism, and anorexia nervosa. In Addi-

*One of these patients became emaciated as a result of carcinoma of the cervix. See FARQUHARSON, R. F., BELT, T. H., and DUFF, G. LYMAN: Simmonds' disease: clinical and pathological observations on four cases. Tr. Am. Climat. & Clin. A. 54:106, 1938.

Figure 4. Patient with anorexia nervosa showing a degree of emaciation seldom seen in Simmonds' disease, yet she was quite alert, active and bright.

son's disease, the characteristic pigmentation of skin and mucous membranes is usually present and is then diagnostic; furthermore, patients with Addison's disease seldom lose axillary and pubic hair. The history of onset of symptoms of hypogonadism and other manifestations of Simmonds' disease, as stated before, usually make the diagnosis clear. If the differentiation cannot be made at once it matters little, for the aim of initial treatment of either condition is the same, namely to relieve the adrenal cortical insufficiency.

It is seldom difficult to distinguish myxedema from Simmonds' disease. Patients suffering from Simmonds' disease usually lack the coarseness of features, the malar flush, deep voice, and thickened skin seen in myxedematous patients. If Simmonds' disease is suspected in a patient presenting symptoms of hypothyroidism, treatment with thyroid gland should be undertaken with great caution, giving small doses (¼ to ½ gr. per day) until the diagnosis is clear, for the administration of larger amounts may bring on a crisis of adrenocortical insufficiency.

Patients suffering from anorexia nervosa are often incorrectly diagnosed as cases of Simmonds' disease. Based on an examination of the lists of outstanding manifestations, the two disorders seem to be similar; in both are found thinness and emaciation, amenorrhea, low basal metabolic rate, low blood sugar, low temperature, pulse, and blood pressure. But they are fundamentally different and the differentiation is easily made if one does not pay too much attention to laboratory findings.

Actually the diagnosis of anorexia nervosa can be made correctly over the telephone. The outstanding characteristic is a morbid aversion to eating, a desire to lose weight which dominates the patient's whole life. It begins usually in the unstable period of adolescence and is commoner in girls. Often the patient has been obese, and almost always unhappy. The desire to lose weight becomes an obsession, and often indulgence in appetite appears to be sinful. Menses may cease before much weight is lost but, even when emaciation is extreme, axillary and pubic hair persist and the breasts may not be atrophic. The blood sugar is not as low as in Simmonds' disease, and the lowering of the basal metabolic rate roughly parallels the degree of emaciation. These patients remain quick, alert, active and restless and often deny ill health until emaciated to a degree not seen in patients with organic disease who are still able to get about. The emaciation becomes more marked than in Simmonds' disease. As Sir William Gull pointed out: "These wilful patients are often allowed to drift their way into a state of extreme exhaustion, when it might have been prevented by placing them under different moral conditions."

TREATMENT

In this brief discussion of the treatment of Simmonds' disease only the general principles of therapy will be considered.

As yet no satisfactory potent extract of the an-

terior lobe of the pituitary gland is available. Accordingly, treatment of patients with Simmonds' disease consists largely in the relief of secondary deficiencies of the gonads, thyroid, and adrenal glands and in the general management and encouragement of the patient. Treatment of adrenocortical insufficiency is most important and may be a matter of emergency. In crisis, it is necessary to relieve the dehydration by liberal administration of solutions of glucose and sodium chloride and to give large amounts of adrenal cortical extract. Later, a routine regimen is developed, using either cortical extract or the synthetic desoxycorticosterone acetate in dosage found necessary, or pellets may be implanted.

When the symptoms of adrenal cortical insufficiency have been relieved, one may begin thyroid therapy giving ¼ gr. per day. The dosage should be increased gradually at long intervals and should always be low; it should be continued only if it proves to be decidedly helpful. The administration of chorionic gonadotropin should relieve the manifestations of hypogonadism and may help in the relief of the weakness and fatigue.

Necessary as treatment of the patient with Simmonds' disease may be, it is obviously more important to prevent its occurrence if possible. The incidence would be reduced if postpartum hemorrhage could be either prevented or treated adequately with transfusion of blood at an early stage to prevent the occurrence of collapse with prolonged severe depression of the blood pressure.

REFLECTIONS OF A HEMOPHILIAC

MR. WILLIAM CAMP (Long Ditton, Surrey) writes: I am a hemophiliac 52 years of age. . . . From my birth until I was over 30 years of age I had spent over twenty years in hospitals. I had almost no schooling and my education was very little, so please forgive me if my writing becomes confused. Apart from this awful hemophilia I don't know what it's like to feel "off color." . . . When I was born my mother was a widow and I was brought up in the world's worst slum tenements. My mother was ignorant about the complaint. I can just remember being booted around and being bashed about. My playthings, I recall, were pieces of broken colored glass and rusty tin cans. Lumme! At 16 I was ready to face the world alone—ignorant, and badly crippled in my legs through continuous painful swellings in my knees. . . .

My mother told me that I was a "bleeder." I didn't quite know what that meant, but I believe that I thought that it was my religion. I soon found out! . . . I am very poor, yet I should bet that no living soul in this wide world has been shown greater kindness and sympathy than I have received from doctors and nurses. If the nurses have been angels to me (and they have, indeed), my doctors have had a very large dose of the "divine" about them. More than half a dozen doctors have pulled me back from the grave. Why? I've been a bloody nuisance to them most of my life. . . . Why do they do it? It's splendid! It's magnificent! It's superb! It's a miracle! It's—being a doctor. It's the quality of God in man. . . .

I can remember now how, about thirty years ago, I had been bleeding for about ten days. Doctor said, I believe, "If it doesn't stop soon I shall have to cut one of your veins and let your blood mingle with his"—he said that to the sister, a sweet, lovely girl. She said to him, "Cut where you like. Start now!" That horrified me. I thought that I'd rather do anything than see her be maimed for me. I couldn't think what to do. So I stopped bleeding. . . .

I remember how a beautiful, wonderful woman fell in love with me about twenty years ago. I told her everything I knew about my hemophilia. She said, "Right, we get married tomorrow." That was the biggest shock of all. She still loves me. . . .

I have a son 18 years of age. He is 6 feet tall and is classified A1 in the Army. . . . Through hard study and a brilliant intellect he has put himself on the road to becoming one of the finest mathematicians in the country one day. . . . Lucky that I had a boy? Shouldn't he have been born? I have another son of 13 years. He has only had measles. I have a third son aged 7. So to the eugenists I would say, "So what?" Lucky to have 3 boys? I don't feel clever over the fact that my children are boys. I'm not clever. Are the eugenists so very hot? . . . I've got through so far—thanks mainly to my wife and to your wonderful profession.

From: British Medical Journal, "Notes and Comments."

Diagnostic Clinic

Diagnosis and Treatment of Surgical Esophageal Lesions

ALTON OCHSNER, MICHAEL DEBAKEY, PAUL DECAMP, WILLIAM B. AYERS, AND LEWELL C. BUTLER*

TULANE UNIVERSITY SCHOOL OF MEDICINE, NEW ORLEANS

Only within the last decade have lesions of the thoracic esophagus been considered of surgical importance and amenable to surgical therapy. Prior to this time a few isolated cases of resection of esophageal lesions, either neoplastic or benign, were reported but these were exceptional. At present, because of the development of newer technical procedures, a better understanding of disturbed physiology in patients suffering with esophageal lesions and the correction of these deficiencies, the availability of better anesthesia, and the introduction of antibiotics, surgery of the esophagus has become not only feasible but also practical.

The present discussion will be limited to the consideration of these lesions which lie within the thoracic portion of the esophagus or the immediately adjacent abdominal esophagus. The three most important esophageal lesions are: (1) carcinoma, (2) benign stricture due either to ingestion of corrosive substances or nonspecific esophagitis, and (3) achalasia.

Esophageal carcinoma, as carcinoma elsewhere, is invasive and destructive, but in common with other esophageal lesions it may kill in a different manner, i.e., by starvation. All esophageal lesions relatively early produce profound nutritional disturbances because of obstruction of the esophageal lumen. This is of importance not only because of the nutritional disturbances themselves but also because of the effect upon the hemopoietic system. Lyons and his associates[20] have shown that in individuals with chronic illnesses, such as infections or neoplasms, particularly if there is loss of weight, there is a contraction of the blood volume which if unrecognized and uncorrected greatly increases the risk of any operative procedure. Undoubtedly many of the earlier failures in esophageal surgery were due to interference with the normal healing of the anastomotic site because of a hemoglobin deficiency which was not recognized because of the contracted blood volume.

Carcinoma of the esophagus is a formidable disease because of the likelihood of early extension of the lesion to adjacent structures within the mediastinum and because of the early metastases to regional lymph nodes. The close proximity of the esophagus to important vital mediastinal structures such as the trachea, the aorta, the pericardium, and vena cava, makes the need for early diagnosis and eradication of the lesion urgent.

Benign cicatricial stenoses of the esophagus, although not attended with the bad prognosis of carcinoma of the esophagus, is an extremely uncomfortable condition because the patient is unable to swallow food and, if the stenosis is severe, there may be an accumulation of saliva in the upper esophageal segment and mouth resulting in overflowing into the trachea and bronchi producing recurrent pneumonitis and bronchiectasis. The latter complications are the most dangerous as regards life.

Achalasia or cardiospasm in which there is either a lack of relaxation in the cardiac end of the esophagus or a spasm and concomitant hyper-

*From the Department of Surgery, School of Medicine, Tulane University of Louisiana, the Charity Hospital of Louisiana, and the Ochsner Clinic, New Orleans, Louisiana.

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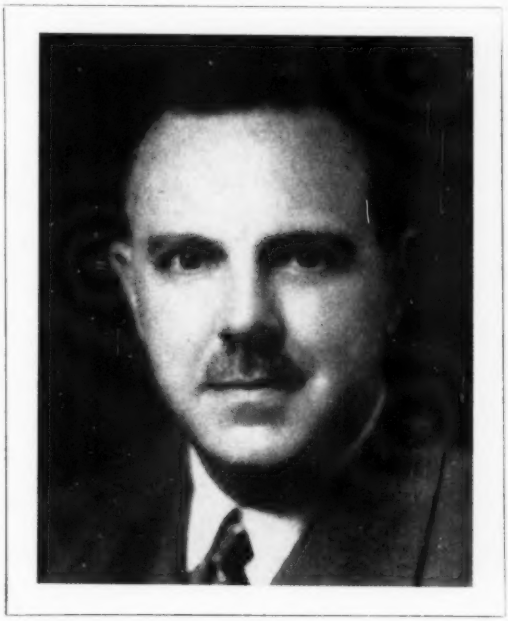
trophy, dilatation, and elongation of the esophagus proximal to the obstructed area often produces serious symptoms.

DIAGNOSTIC PROCEDURES

Accurate diagnosis of esophageal lesions is usually possible because the esophagus lends itself exceptionally well not only to indirect visualization by means of roentgenography following ingestion of contrast substances but also to direct visualization by esophagoscopy. Roentgenography, because of its simplicity, can be done easily and usually without any danger unless there is complete obstruction, particularly in an infant in whom there is danger of aspiration of the ingested material. If such a possibility is considered it is advisable to use a contrast substance such as lipiodol which is not irritating to the tracheobronchial mucosa as is barium.

By means of fluoroscopic observation of the passage of the contrast substance through the esophagus the roentgenologist can determine changes in contour, alterations in the outline of the esophageal mucosa, and evidence of obstruction. Frequently he is able to predict the type of lesion involving the esophagus. Although definitely more hazardous than roentgen examination of the esophagus, esophagoscopy is even more valuable as a diagnostic procedure because it not only permits direct visualization of the lesion but generally permits the removal of a piece of tissue for microscopic examination. If no suspicious lesion is seen which lends itself to biopsy, the aspiration of esophageal secretion for cytologic examination is of value.



ALTON OCHSNER

INCIDENCE

The incidence of carinoma of the esophagus appears to be increasing. Although formerly considered rare, it now ranks as ninth most frequent malignant tumor occurring in the white male.[6] In the United States the reported deaths from cancer of the esophagus increased from 2,243 to 2,949 from 1934 to 1944, an increase of approximately 30 per cent.

Carcinoma of the esophagus is primarily a disease of advancing age. In a series of 235 cases which we observed, the greatest incidence was in the seventh decade (36.6 per cent); 30.6 per cent were in the sixth decade and about an equal number were in the fifth and eighth decades (14.1 per cent and 13.2 per cent, respectively); 3.8 per cent were in the fourth decade and 1.7 per cent in the ninth decade (Chart 1). Although incidence of esophageal carcinoma is increasing it is not as great as the increased incidence of bronchiogenic carcinoma (Chart 2).

There is no racial predisposition to esophageal carcinoma. In our series of cases, 172 were observed at the Charity Hospital, an institution to which both white and colored patients are admitted with about equal frequency. Of this group 79 (45.9 per cent) were white and 93 (54.1 per cent) were colored (Chart 3). It is generally a disease of men. In our series 68.6 per cent were in men and 31.4 per cent in women. It is of interest that of the 69 cases seen in private practice, a greater percentage were in females (64 per cent); whereas of the Charity Hospital cases, 80 per cent were males and 20 per cent females. The reason for this discrepancy between the private practice and the Charity Hospital series is not obvious.

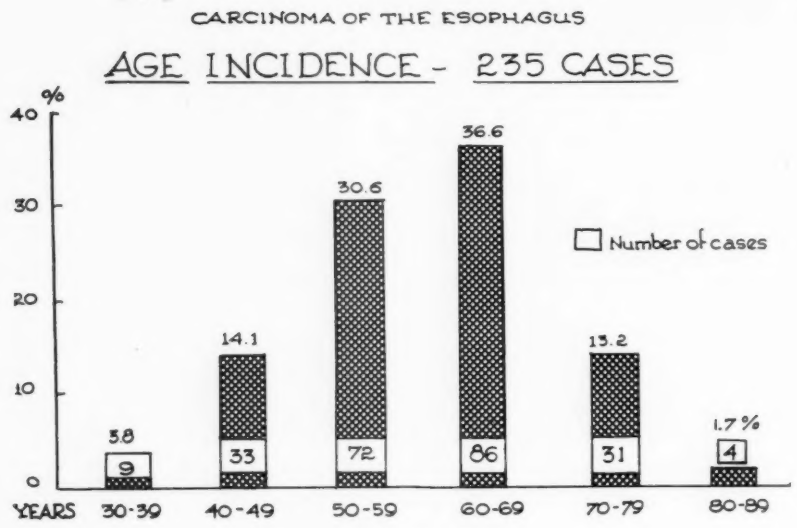


CHART I

ETIOLOGY

THE etiology of esophageal malignancies is not known, although in all probability chronic irritation is of significance. The higher incidence of esophageal carcinoma among the Orientals, particularly Chinese, is thought to be due to the irritative effect of the ingestion of large amounts of extremely hot tea by these people. Undoubtedly the presence of gastric cell rests in the lower end of the esophagus is a factor in the development of malignancy in this region since gastric mucosa is particularly susceptible to malignant change.

SITE OF ESOPHAGEAL CARCINOMA

Most carcinomas of the esophagus are found in the thoracic portion, although the lesion may be situated in any part of the cervical or thoracic esophagus. In a collected series of 1,670 cases of carcinoma of the esophagus, Janeway and Green[17] found that almost 85 per cent of the lesions occurred in the middle and lower thirds of the esophagus. We found in a collection of 8,572 cases[29] that 80 per cent were in the thoracic or abdominal esophagus. Carcinoma of the esophagus therefore becomes largely a problem of the thoracic surgeon.

There are two recognized histologic types of carcinoma of the esophagus, the squamous cell type and the adenocarcinoma. Squamous cell carcinoma, which is the more common, arises from the squamous epithelial lining of the esophagus and can be found in any part of the esophagus. It is usually ulcerative and shows a tendency for proliferative growth near its borders and submucosal extension beyond its apparent peripheral limits. Because of this submucosal extension, it is imperative in performing an esophagectomy that wide resection is done in order to insure removal of the entire lesion.

Adenocarcinoma is usually located in the lower segment of the esophagus. It may arise in the gastric mucosa and extend up into the esophagus; on the other hand, it may originate in islands of misplaced or aberrant gastric mucosa which are found most frequently in the lower part of the esophagus.

As mentioned before, carcinoma of the esophagus is associated with a high degree of malignancy and because of this it rapidly invades adjacent structures, most of which are vitally important. In addition to this, because of the early obstruction of the esophagus, there is interference with the passage of food into the stomach followed by emaciation and progressive deterioration of the individual. Carcinomas of the esophagus metastasize early to the regional lymph nodes. In the mid-portion and lower portion of the esophagus the lymph nodes in the region of the hilum of the

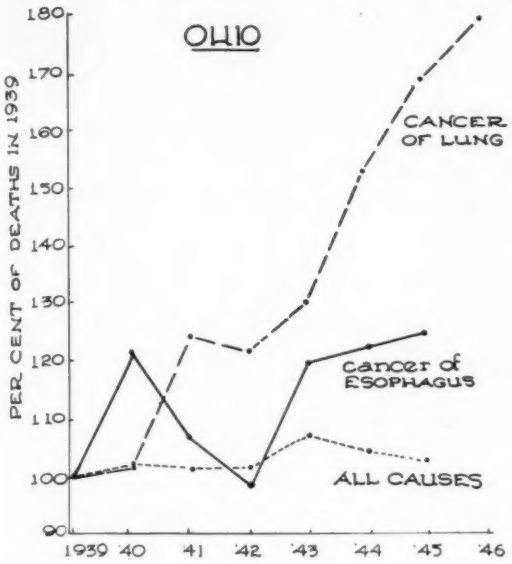


CHART 2

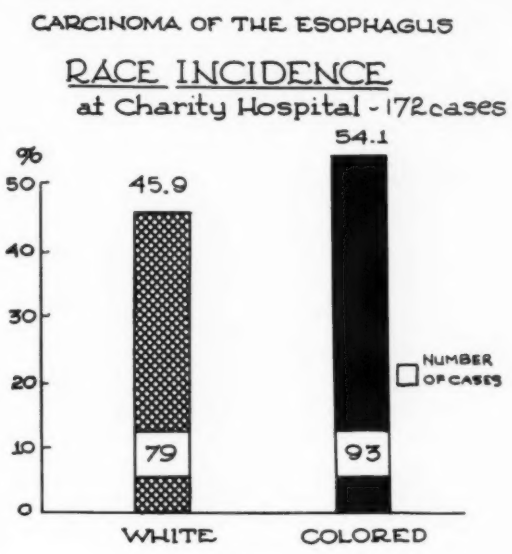


CHART 3

lung may be involved and must of necessity be removed in performing an esophagectomy. In the lesions involving the lower esophagus, metastases to the lymph nodes in the region of the cardia, the gastrohepatic ligament, and around the left artery are frequent. Metastasis to the liver of lesions of the distal esophagus is also possible.

CLINICAL MANIFESTATIONS

The clinical manifestations of esophageal carcinoma are in the beginning vague and indistinct. Because of their vagueness and intermittent character they are likely to be disregarded by the patient and even too frequently by the physician. The importance of the early manifestations of esophageal carcinoma cannot be overemphasized because it is at this time when the diagnosis should be made because therapy is more successful if instituted before late manifestations occur.

The early symptoms consist of a vague sensation of oppression or fullness in the thoracic or substernal area, epigastric distress, heartburn, increased salivation, usually associated with the ingestion of food and frequently disappearing after a meal. Such symptoms occurring in an individual, particularly a male, past 40 years of age should be suggestive of an esophageal lesion and make mandatory an investigation of the esophagus to exclude an early malignancy. Salivation is a symptom commonly found in all esophageal lesions and it frequently occurs before there is any obstruction to the lumen of the esophagus.

After several months of the vague complaint the symptoms become progressive and definite dysphagia appears which is usually due to a narrowing of the lumen of the esophagus. The dysphagia in esophageal carcinoma is characteristically progressive in that in the beginning there is difficulty in eating large pieces of solid food, such as meat. If allowed to go on, there is progressive difficulty in eating first, smaller particles of solid food, then soft foods, and finally liquids.

THE progressive picture should never be allowed to develop, however, because a diagnosis should be made and definitive therapy instituted long before the lesion has extended to such a degree. With the increasing dysphagia there is anorexia and loss of weight. Regurgitation of food from the dilated segment above the obstruction relieves the patient and is frequently resorted to. Finally dehydration and hematemesis may occur

but they usually indicate a terminal phase of an esophageal carcinoma.

As mentioned before, the diagnosis of esophageal carcinoma and other esophageal lesions is not difficult if only the possibility of its existence is considered and appropriate diagnostic measures used. Esophagograms and visualizations of the esophagus under fluoroscopic observation are important, but even when they are negative the persistence of symptoms referable to the esophagus demands esophagoscopy performed by one who is adequately trained in performing this diagnostic procedure. By means of esophagoscopy, direct visualization of the tumor is possible and with few instances a piece of tissue can be obtained for microscopic examination. If no obvious lesion is seen which can be biopsied, the esophageal secretion should be aspirated and carefully examined for malignant cells.

CURATIVE TREATMENT

The only curative treatment of carcinoma of the esophagus is removal of the involved portion of the viscus. Other therapeutic measures are at best only palliative. Until relatively recently surgical extirpation of the esophagus was not considered safe and not considered feasible and because of this most cases of carcinoma of the esophagus were treated by other therapeutic measures, particularly x-ray therapy. Results have not been satisfactory.

In a series of 297 cases reported by Natherson and Welch[27] it was found that the medium life expectancy of untreated patients with esophageal carcinoma was 7 months, of those treated by gastrostomy, 10.4 months, and of those treated by irradiation, 9.3 months. Watson[37] reported that the average life expectancies in cases treated by gastrostomy and external irradiation, gastrostomy and internal irradiation, and gastrostomy and internal and external irradiation were 6.3, 3.7 and 3.9 months respectively. Zuppinger[41] found that the difference in survival periods found in those treated and those not treated was 0.3 months. Cleminson and Monkhose[4] found that the average survival period following irradiation was 5.6 months.

In 1938 Adams and Phemister[1] reported a successful resection of a carcinoma of the esophagus through a thoracic incision and described the technic which has been widely adopted. Since that time there has been a marked broadening in the indications for resection of esophageal malignant lesions and although lesions located in the upper part of the esophagus were thought to be not amenable to surgical extirpation and reestablishment of the continuity of the digestive tubes, such now is not only feasible but is being done very extensively. Prior to that time lesions in the upper part and mid-portions of the esophagus were treated by procedures based upon the principles of the old Torek operation[34] with subsequent multistaged antithoracic esophagoplasties for restoration of continuity of the alimentary tract. In 1944 Garlock[8] and Sweet[32] demonstrated that the stomach could be adequately mobilized to bring it to the highest levels in the chest permitting anastomosis with the esophagus with immediate restoration of function.

IMPORTANCE OF BLOOD VOLUME DEFICIENCY

As referred to earlier, in the beginning the results following esophagectomy for carcinoma were quite unsatisfactory, probably because of a number of factors. One of the most important was the failure to recognize blood volume deficiency which occurs so consistently in these individuals and its consequent effect on wound healing. Lyons[20] has shown that the chronically ill patient, particularly one who has lost weight, usually has a contracted blood volume and an anemia which is not demonstrated by the ordinary blood determinations. Although the red cell count per cubic millimeter and the hemoglobin percentage may be within normal limits because of a hemoconcentration accompanying the blood volume deficiency, a severe anemia can exist.

The importance of the diminished blood volume is obvious when one considers the magnitude of the operative procedure necessary and the associated operative trauma accompanying esophagectomy for carcinoma. Although the normal individual with a normal blood volume might be able to withstand the same degree of trauma with little danger, an individual whose blood volume is diminished because of debilitating conditions may go into shock relatively early in the course of the procedure just as the experimental animal with acute blood volume deficiency is unable to stand much trauma.

Uncorrected blood volume deficiency is serious not only because of the danger of the development of shock, but also because of the associated

uncorrected anemia which is likely to delay wound healing. As demonstrated by Whipple,[39] in anemia there is a preferential demand upon available protein stores for the synthesis of hemoglobin. If the plasma proteins are utilized for synthesis of hemoglobin in an individual with a hemoglobin deficiency, the proteins necessary for the healing of an anastomotic wound following esophagectomy may not be available and an insufficiency at the suture line is likely. We have repeatedly found in patients with esophageal carcinoma that the hemoglobin percentage values may be within normal limits, i.e., 80 per cent to 90 per cent, whereas in the same individual the total hemoglobin values are less than 40 per cent of normal.

In a series of 10 cases of esophageal carcinoma in which blood volume determinations were made and the actual determinations of the total cell mass and total hemoglobin values were made, the importance of blood volume determinations became evident. In the 10 cases the average values were as follows: body weight, 83 per cent of normal; blood volume, 73 per cent of normal; plasma volume, 93 per cent of normal; total protein, 83 per cent; the total cell mass, 50 per cent; and the total hemoglobin, 45 per cent of normal.

We are convinced after considerable experience with the operative treatment of patients with esophageal carcinoma that careful determinations of blood volume preliminary to the operation are necessary because only in this way can the degree of anemia accurately be determined. The amount of blood required preoperatively to correct the blood volume deficiency varies considerably. In 89 cases of chronically ill patients in whom blood volume deficiencies were determined preoperatively it was found that the smallest amount of blood required to correct the deficiency was 1,500 cc., the largest amount was 4,000 cc. and the average was 2,700 cc. The shortest length of time required to correct the deficiency was three days, the longest was eight days, and the average was five days.

Although the correction of anemia and blood volume deficiency is important in all chronically ill patients before an operative procedure is undertaken, it is particularly important in a patient with esophageal lesions because of the difficulty of oral feeding and because of the impossibility of reestablishing protein balance by normal alimentation. This can be accomplished, however, relatively simply and quickly by means of administration of adequate amounts of whole blood.

ANESTHESIA

Of great importance also in permitting the extirpation of extensive esophageal lesions safely is competent anesthesia. A well trained anesthetist who is familiar with anesthesia of patients undergoing thoracic operations is necessary for the successful performance of an esophagectomy and unless available, esophageal surgery should not be undertaken.

TECHNIC OF ESOPHAGECTOMY

The technic of esophagectomy depends largely upon the location of the lesion. A lesion in the distal portion of the esophagus is satisfactorily exposed through an incision over the left eighth rib or in the eighth intercostal space. If the symptoms have been present for a long period of time, it is probably desirable to make a preliminary abdominal incision, either transversely or longitudinally as suggested by Garlock[9] in order to explore the abdomen to determine whether the tumor has extended into the abdomen.

Low lying lesions which have existed for many months are likely to extend to the lymph nodes of the cardia, the gastric hepatic omentum, the nodes around the celiac axis, and to the liver. Although hepatic involvement need not necessarily preclude resectability because it is becoming increasingly accepted by thoracic surgeons that even palliative resection of carcinoma of the esophagus is justified in order to permit the patient to swallow normally and to free him of the lesion which is producing his symptoms, if there is involvement of vital structures, such as the celiac axis, resection should not be done. A palliative gastrostomy can be done.

In the event that no involvement of the abdominal viscera is found or involvement is such that a palliative resection can be done, the incision is extended across the costal margin to the left sixth or seventh interspace, opening the thorax also. The diaphragm is incised down to the esophageal hiatus. This permits a wide exposure not only of the abdominal viscera but also those of the lower thorax. On the other hand, if symptoms have been present for a relatively short period of time, the low lying lesion is probably best approached through a thoracic incision dividing the diaphragm by means of an incision extending out from the

esophageal hiatus laterally. The stomach can be mobilized upward and an adequate portion of the esophagus and adjacent stomach removed to permit extirpation of all of the involved esophagus together with a wide portion beyond. The continuity of the digestive tube is reestablished by anastomosing the distal end of the esophagus to the anterior wall of the stomach.

In order to prevent subsequent stricture, we suggested and have continued to use a technic which permits the formation of a large opening. A longitudinal incision is made on one side of the esophagus greatly increasing the size of the opening. An L-shaped incision is made in the anterior wall of the stomach corresponding to the incision in the esophagus. The anastomosis is made utilizing two layers of interrupted sutures of quilting cotton. Finally the stomach is sutured to the thoracic parieties and the opening in the diaphragm is closed around the stomach.

The treatment of the high lying lesions, those in the mid-portion of the esophagus or above, is more difficult because of the necessity of the mobilization of the retro-aortic portion, bringing it anterior to the aorta, and the removal of practically all of the thoracic esophagus.

Because of the resection of practically all the thoracic esophagus extensive mobilization of the stomach is necessary in order to permit it to be brought to the upper part of the pleural cavity. The mobilization is obtained by division of the gastrolienal, gastrocolic, gastrohepatic ligaments and their vessels, care being taken to preserve the vascular arches along the greater and lesser curvatures. This is followed by division of the left gastric artery close to its origin and complete removal of the lymph nodes in this region. This must be done with utmost gentleness and care in order to avoid injury to the intramural vessels because the entire blood supply to the stomach is derived only from the right gastro-epiploic and the right gastric arteries. It is usually necessary to mobilize the stomach further by incising the peritoneal covering just to the right of the duodenum, permitting mobilization of the duodenum and pylorus to the left.

Following mobilization of the stomach the esophagus is divided well above the tumor in order to permit adequate excision of the neoplasm and esophagogastrostomy is done above the arch of the aorta in a manner similar to that used for low lying lesions. The stomach is sutured to the lateral parieties of the chest wall and the opening in the diaphragm is closed around the esophagus. The thoracic cavity is closed after introducing a long catheter in the posterior gutter to be used for drainage. The catheter is removed after the lung is completely reexpanded.

Postoperatively the patient is given oxygen, continued suction is maintained on the catheter drainage tube, and antibiotic therapy begun. Although originally we used penicillin postoperatively we now use "blitz therapy" which consists of the administration of penicillin, sulfonamides, and streptomycin. The reason for the combination of the three agents is that occasionally when using a single chemotherapeutic agent or antibiotic, infection develops because of resistance of a particular organism to the agent. By the combination of all three, those microorganisms which might be resistant to one will probably be susceptible to others and will be inhibited before they have a chance to grow and get a foothold. Since using this therapy we have seen practically no cases of infection.

During the first several postoperative days parenteral fluids and blood are administered as required. It is important to prevent atelectasis and pneumonitis by encouraging deep breathing and expectoration of retained secretion. Although some surgeons prohibit drinking early in order to provide immobilization at the site of anastomosis, we have observed no undesirable effects from this and have permitted the patients to drink fluids, usually tap water, as soon as they have recovered from the anesthetic.

Suction attached to an intranasal gastric tube introduced through the anastomotic site at the time of operation will keep the stomach deflated. The tube is usually removed by the third or fourth postoperative day when intestinal peristalsis is returned and small feedings can be started. Early ambulation is encouraged and most patients are out of bed by the fourth or fifth day.

RESULTS

Unfortunately the results in carcinoma of the esophagus are still very bad and will continue to be so until earlier diagnoses are made which will permit curative procedures to be instituted at a time when the lesion is resectable and curable. Of 244 cases of esophageal carcinoma which we have seen, 159 (65.2 per cent) were not explored either because they were obviously in-

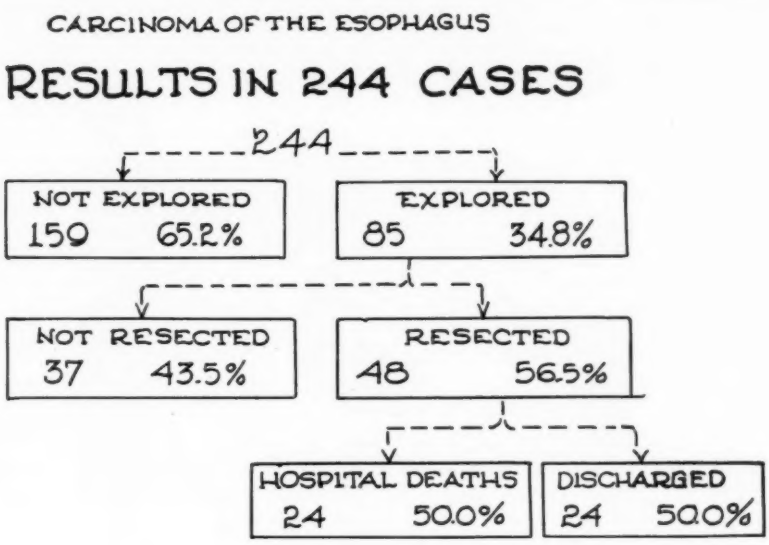


CHART 4

operable because of extension beyond the esophagus or because the patient refused operation (Chart 4). Eighty-five (34.8 per cent) were explored. Of the 85 explored, 37 (43.5 per cent) were not resectable because of the extent of the lesion. Forty-eight (56.5 per cent or 19.7 per cent of the entire group) were resected. Of the 48 resected, 24 died within the hospital (mortality rate of 50 per cent).

Although these figures are anything but satisfactory there is some reason for optimism when one considers what has been accomplished since 1947. The incidence of exploration in the entire group was 34.8 per cent; before 1947 it was only 29 per cent and since 1947, it was 61 per cent (Chart 5). Also the resectability of the entire group of cases has increased in more recent years, partly due to the fact that palliative resections are now being done, but also in part due to the fact that cases are seen relatively earlier. Whereas the incidence of resection in the entire group of cases was 19.7 per cent, before 1947 it was only 16 per cent; since 1947 it has been 36.4 per cent (Chart 6). The incidence of resectability in the cases in which exploration was done has remained about the same. In the entire group of cases which were explored, the incidence of resectability was 56.5 per cent; in the group explored before 1947 the incidence of resectability was 55.2 per cent, and in the group explored since 1947 the resectability was 59.3 per cent (Chart 7).

Although a 50 per cent hospital mortality rate is extremely high and is much higher than it should be, it can be and will be reduced when cases are operated upon earlier. The mortality rate in cases operated upon before 1945 was 75 per cent whereas since 1945 the mortality rate was 37.5 per cent (Chart 8).

BENIGN ESOPHAGEAL STRICTURES

Benign strictures of the esophagus are relatively rare and are becoming increasingly less frequent because of the prevention of lesions which cause cicatricial contracture. With the educational program conducted largely by otolaryngologists accidental ingestion of corrosive substances has largely been prevented. Suicidal intent is occasionally responsible for ingestion of corrosive substances. Cicatricial stenosis of the esophagus following acute esophagitis either because of regurgitated acid gastric chyme or associated with short esophagus with the consequent inflammation of the thoracic portion of the stomach and the adjacent esophagus is relatively rare.

Another reason for the decreasing frequency of benign strictures is that even when acute esophagitis following ingestion of corrosing substances or nonspecific inflammations occurs, stricture is usually prevented by

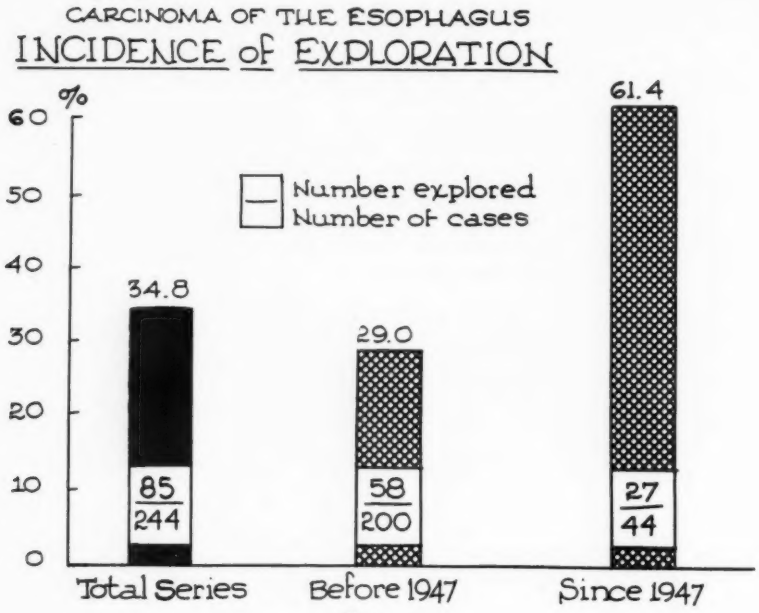
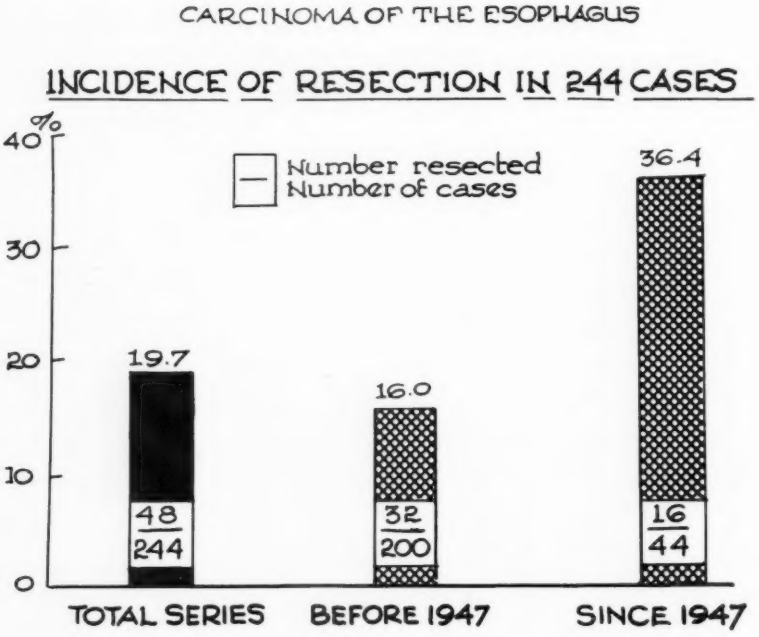


CHART 5



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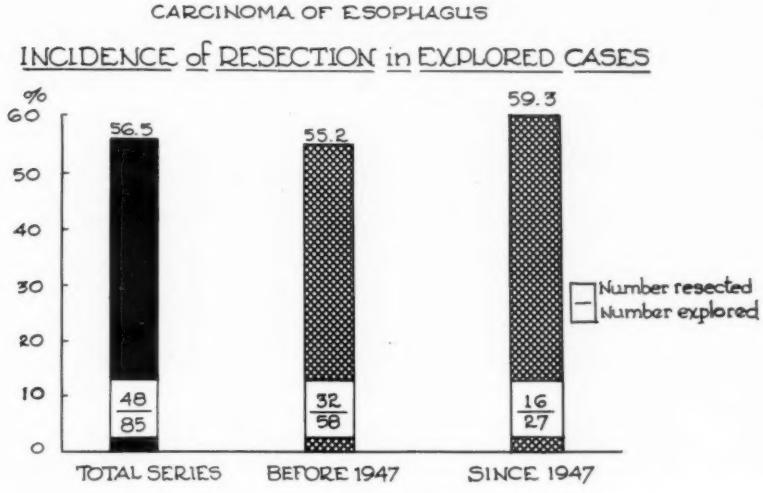

CHART 7

adequate early bougienage. It is only after a high grade stricture has developed, usually due to neglect during the course of the esophagitis, that the condition becomes of surgical importance.

The clinical picture of benign stricture following esophagitis consists of progressive dysphagia which has been present for some time. If the stricture is marked there is the likelihood of accumulation of secretions proximal to the obstruction which can overflow into the larynx, trachea, and bronchi with the development of atelectasis, pneumonitis, and bronchiectasis. Esophageal strictures are therefore important not only because of interference with nutrition but also because of the more serious pulmonary complications.

The diagnosis of benign esophageal strictures is usually not difficult because generally there is a history of an acute esophagitis following either the ingestion of corrosive substances or a nonspecific inflammatory lesion. Careful examination of the esophagus both by x-ray and esophagoscopy is of importance because the benign esophageal lesions may simulate a carcinoma; in fact, it is possible that a carcinoma may develop in an esophagus in which there has been a long standing obstruction as a result of a cicatricial stenosis.

Resection of the esophagus is frequently indicated in severe benign stenosis of the esophagus in order to relieve the patient not only of obstructive manifestations of the esophagus but also to prevent respiratory complications. Even though the esophageal lesion may be relatively short, as it frequently is, it is usually necessary to remove all the esophagus distal to the stenosis because the relative fixation of the esophagus and the short length of the esophageal arteries prohibit sufficient mobilization of the unresected portion of the esophagus to permit a reestablishment of its continuity. As in esophagogastrostomy for carcinoma the stomach is mobilized and an anastomosis performed upward. The procedure is generally much simpler and associated with less risk than in carcinoma for several reasons. First, the patient is usually younger and is able to withstand an operation of the necessary magnitude. Second, generally the esophagus can be mobilized more readily. At times, however, there are extensive periesophageal adhesions resulting from a severe periesophagitis accompanying the original esophagitis.

CONGENITAL STENOSES

Congenital stenoses may occur although the most frequent congenital esophageal lesion is esophageal atresia with fistulous communication between the distal esophageal segment and the trachea or bronchi, and it is not the purpose of this discussion to include these lesions. Congenital esophageal stenoses produce symptoms which are quite similar to those caused by benign acquired cicatricial stenosis following esophagitis. The principal difference is that dysphagia begins shortly after birth in congenital stenosis.

We have operated upon three cases of cicatricial stricture following esophagitis caused by chemical corrosion of the esophagus which have necessitated resection of the esophagus and one case of congenital stricture of the esophagus caused by a web. The three cicatricial stenoses were treated by esophagectomy and esophagogastrostomy, all with excellent results. The patient with the congenital web was treated by esoph-

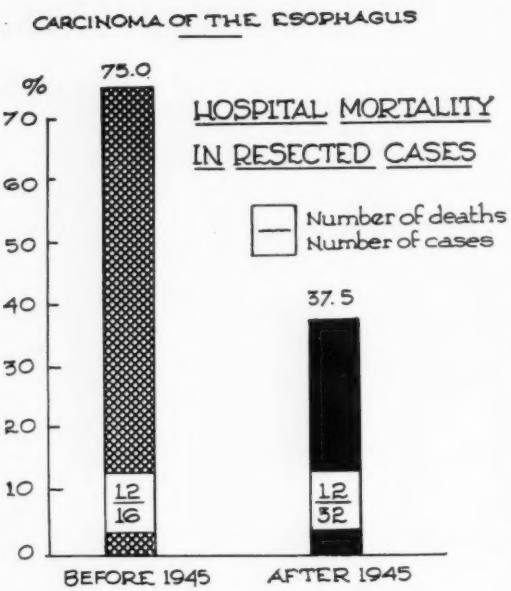

CHART 8

agotomy and excision of the membranous band which acted as a valve, completely obstructing the lumen of the esophagus at times and other times perverting the passage of some food. The result in this case was also good.

ACHALASIA OF THE ESOPHAGUS

ACHALASIA of the esophagus is a clinical syndrome which is characterized by dilatation, hypertrophy, and elongation of the esophagus associated with obstruction in the region of the cardia or slightly above it. It has been designated by a number of terms which include achalasia, cardiospasm, phrenospasm, idiopathic dilatation of the esophagus, esophagectasia, hiatal esophagismus, megaesophagus, simple ectasia of the esophagus, preventriculosis, dilatio ingluviformis esophagi, dilatio fusiformis and dolichoesophagus. Although there are a number of theories which have advanced to explain the development of this condition, we agree with Einhorn[7] who in 1888 concluded that the cardia in this condition probably fails to open reflexly during the act of deglutition. Hurst,[15,16] the British gastroenterologist, deserves credit for popularizing this conception and for giving it the designation achalasia.

Achalasia is not a particularly common disease of the esophagus but it comprises about 17 per cent of all esophageal lesions.[36] It is the most common lesion producing symptoms of the esophagus in young people. It occurs primarily in neurotic young women and undoubtedly its origin is on a functional basis. Because of the functional character of achalasia, psychotherapy is extremely important in its treatment and in most instances relief can be obtained by conservative measures such as repeated dilatation, either by means of a weighted bougie or by hydrostatic or pneumatic dilators.

However, approximately 25 per cent of cases of achalasia do not respond sufficiently to conservative measures to justify their continuation. If conservative therapy is continued complications resulting from esophagitis are likely to occur and even death may result from a complicating mediastinitis. There has been an erroneous impression that surgical therapy of achalasia entails a considerably greater risk than conservative therapy. Actually the mortality rate of the former is only slightly greater than of the latter. Moersch[26] reported a mortality rate of 2.8 per cent in 804 patients with achalasia treated conservatively whereas in 239 collected cases in which cardioplasty and esophagogastrostomy were performed we found the mortality rate was 4.2 per cent.[28] A large number of surgical procedures have been advocated for the correction of achalasia in those cases in which conservative therapy has not been adequate to relieve the patient's symptoms. If the exact etiology of achalasia were known it might be possible to correct the underlying lesion, but such has not been possible up to the present time.

Because achalasia has been thought by some to be the result of dysfunction of the nerve supply to the esophagus and to be similar to megacolon, it has been suggested that the nerve supply to the esophagus might be attacked surgically. In 1911, Meyer[23] performed vagotomy in addition to esophagoplication, but he was unable to obtain good results and this has been the experience of others. There has been only one satisfactory result in 11 collected cases in which vagotomy was performed as originally reported by us.[30] Recalde[31] was probably the first to attack the sympathetic supply to the esophagus. In 1924, he reported good results in 3 of 4 cases in which decortication of Auerbach's plexus was performed. These clinical observations were confirmed experimentally ten years later by Knight,[19] who demonstrated the presence of a two-sphincter mechanism at the cardia. He further showed that bilateral vagal section reproduces the clinical and pathologic picture of achalasia and that sympathectomy relieves the condition. Based on his observations that in a human being the sympathetic supply to the cardiac sphincter is derived chiefly from the left side of the celiac plexus and distributed along the left gastric artery, he advocated sympathectomy by excision of this artery and the surrounding fat and nervous tissue. Of 5 patients treated in this way, he reported complete relief in one, considerable improvement in one, and recurrence in three. Results of this method reported by others since then

have not been impressive. Craig, Moersch, and Vinson[5] obtained good immediate results in a patient with achalasia by bilateral resection of the cervicothoracic sympathetic ganglia, but a few weeks later there was complete recurrence. We have had one case in which sympathectomy was done with complete failure of improvement.

The other operative procedures employed for achalasia are directed toward (1) the dilated esophagus, (2) the cardia, and (3) the diaphragm. Procedures directed toward the dilated esophagus are obviously illogical and are merely of historical interest. A more rational approach would be one directed toward the cardia since the food ingested meets obstruction at this point. Dilatation of the cardia has been practiced as a conservative treatment for many years and is successful in relieving most cases of achalasia. It is of interest that forceful transgastric manual dilatation of the cardia has been used a good deal in many of the European clinics. This was first advised by von Mikulicz in 1903.[24, 25] However, there seems no advantage in manual dilatation of the cardia over dilatation by the natural oral route.

Plastic procedures on the cardia have been performed for a number of years. Gottstein[11] first proposed an extramucous cardiomyotomy because he believed that there was a true spasm of the cardiac sphincter, but this was not actually performed until twelve years later by Heller.[13] We were previously able to collect 104 cases in which this procedure was done. The results were reported as good in 76.9 per cent, improved in 5.4 per cent, 13.4 per cent had recurrences, and 3.8 per cent of the patients died.

Another plastic procedure on the esophagus is one which is similar to pyloroplasty and consists of a longitudinal incision through the entire wall of the cardia and transverse closure. This was first suggested by Marwedel,[21] but was performed seven years later by Wendel.[38] Of the 36 cases which we collected from the literature and in which cardioplasty was done, good results were reported in 93 per cent, recurrences in 2.8 per cent, and a mortality in 2.8 per cent.

The operation which we prefer is esophagogastrostomy. This consists either of longitudinal incision in the esophagus and the adjacent portion of the fundus of the stomach or a curved incision, beginning in the esophagus, extending through the cardia, and on to the adjacent portion of the stomach. In both, an anastomosis is made between the dilated esophagus and the stomach. In the former, the cardiac orifice is short-circuited whereas in the latter the procedure is similar to a Finney gastroduodenostomy. Heyrovsky,[14] in 1912, originally advocated esophagogastrostomy with an incision through the esophagus into the stomach. In 1940, we collected 97 cases of esophagogastrostomy. Since this time there have been 56 additional cases reported.[3, 10, 12, 18, 22, 33] We have done 4 of our own. Of the total of 157 cases, 150 had good results (95.5 per cent), 5 died (3.1 per cent), and 2 (1.2 per cent) had poor results.

Esophagogastrostomy for cardiospasm can be done either transthoracically or transabdominally. In those cases in which there is marked elongation of the esophagus, which is usually present in true achalasia, it is our belief that the operation can be performed best transabdominally. By the mobilization of the esophagus, one can secure a length of 12 to 15 cm. of the esophagus in the abdomen which permits the performance of the anastomosis between the esophagus and the stomach without any difficulty. The procedure is greatly facilitated by division of the left lateral hepatic ligament to prevent retraction of the left lobe of the liver. In those cases in which the esophagus is not elongated, it is easier and therefore better to perform the operation above the diaphragm.

It is of interest that although good results have been obtained in all but very few patients in whom an esophagogastrostomy has been done, in many instances there is not a decrease in the size of the esophagus following the production of a large opening between the esophagus and the stomach. Wooler[40] is opposed to esophagogastrostomy, because he believes it predisposes to regurgitation of the gastric contents, particularly when the patient is lying down. He has not done the procedure, but prefers the cardiomyotomy. We have never observed regurgitation in our patients following esophagogastrostomy.

Operations directed toward the diaphragm are based on the opinion that the condition is the result of failure of relaxation or incoordination of the diaphragmatic crurar. Bassler[2] suggested division of the diaphragmatic crurar, but Vampre[35] concluded that it is irrational, and he consistently obtained poor results.

On the basis of our own experience and from an evaluation of the reported cases, we believe that esophagogastrostomy is the operation of choice in those cases of cardiospasm in which some type of surgical relief is indicated.

SUMMARY AND CONCLUSIONS

Esophageal lesions although previously thought not to be amenable to any surgical correction, at the present time due to the development of adequate surgical technic, the ability to correct disturbed physiologic processes occurring in individuals with esophageal lesions, the availability of good anesthesia, the availability of antibiotics, and chemotherapeutic agents, are correctable. Unfortunately, malignant lesions of the esophagus generally are diagnosed late. Only by subjecting patients with symptoms referable to the esophagus to roent-

gen examinations and to esophagoscopy can these lesions be detected at a time when a curative procedure can be done relatively safely. The removal of the entire thoracic esophagus with the reestablishment of the continuity of the digestive tube is feasible and practical.

Benign strictures of the esophagus regardless of their cause are also amenable to surgical extirpation followed by esophagogastrostomy.

About 25 per cent of cases of achalasia do not respond to conservative therapy, necessitating surgical relief. Esophagogastrostomy, done either transabdominally or transthoracically, is the therapeutic method of choice.

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EXPERIMENTAL

New Instrument for Administering Penicillin and Streptomycin

NATHAN STEINBERG

PHILADELPHIA

The development of penicillin and streptomycin as valuable antibiotic agents simultaneously created a problem as to the best method of their administration.

In milder disorders the introduction of a mixture of penicillin in oil and wax, and more recently of procaine penicillin in oil or in aqueous solution has made it possible to limit the administration of penicillin to a single daily injection. Here, however, a prolongation of the presence of penicillin in the blood for as long as twenty-four hours is sacrificed for a high intensity bacterial effect obtained by frequent injections.

Since there is no general agreement as to the required concentration of penicillin for the best therapeutic effects, it is deemed best to maintain high plasma levels, especially in diseases due to the more virulent bacterial agents. D'Abreu and his associates[1] express the belief that if no response is apparent in forty-eight hours in the treatment of hand infections, the administration of penicillin in oil and wax should be abandoned. This recommendation must be followed in other diseases similarly treated at the onset, and aqueous penicillin therapy substituted instead.

The parenteral administration of aqueous penicillin at frequent intervals, however, has three obvious disadvantages: (1) the pain of repeated punctures; (2) the necessity and expense of trained personnel to administer the drug; and (3) the great difficulty of obtaining such trained nursing care, either in the home or hospital.

Many efforts have been made to eliminate some of these disadvantages. Edwards[2] describes an apparatus consisting of a chest aspirator and a bottle containing the twenty-four-hour dosage attached to a constant indwelling needle. That patients welcome any method which obviates repeated needle punctures is shown by the work of Turton[3] who describes a continuous drip apparatus with the needle in situ, in which 24 of 30 patients treated preferred such a technic as compared to 6 who disliked the continuous sensation of a needle and complained that their movements were hampered by the apparatus. Barnard[4] and Last[5] have reported on the use of a clock mechanism, driving a toothed rack or threaded screw, respectively, to push forward a plunger of a syringe containing the twenty-four-hour penicillin dosage. Finally, both Freeman[6] and Salz[7] describe almost identical methods of continual implantation of a needle in the thigh for intramuscular administration.

The above methods are impractical for the most part, because of the expense involved, the bulkiness of the apparatus making ambulation almost impossible, and the technical difficulties requiring the attendance of trained personnel.

Efforts by Kolmer and his co-workers[8] to prolong the action of streptomycin by means of a mixture in oil and wax, ended in failure.

In the absence of a better method of streptomycin administration, a number of physicians have been giving the required twenty-four-hour dose as a single daily injection. When administering 1 gm.

of streptomycin or more daily this undesirable technic increases the frequency and severity of toxic reactions and should be avoided.

To overcome these problems an instrument was devised which is simple in construction, light in weight, relatively inexpensive, and which permits the patient to self administer the antibiotic at definite intervals either at home or in the hospital, once the apparatus is applied by the physician. It is a mechanism which fits about a 6 cc. syringe, attached to a curved needle implanted in the tissues and permits ½ cc. doses to be instilled when the lever is released and the plunger is pushed forward by hand.

DESCRIPTION

The Multidose Injector consists of three removable parts (see Figure 1): (1) the syringe holder, fitting about the barrel of the syringe; (2) the sandwich clasp which embraces the head of the plunger, and (3) the wire rack which fixes the instrument onto the patient's body.

The syringe holder is composed of (a) a circular piece and lateral extending finger grasps, which embraces the flange of the barrel and is held in place by a pivoted flat spring (F.S.). An opening in the center of this flat spring through which the plunger rides, aids in holding the instrument on the barrel of the syringe; (b) a lever (L) pivoted between two parallel plates attached perpendicular to the circular piece. At each end of this lever are sawtooth-like projections which butt against successive similar projections on the ratchet (R). This lever is held firmly in one of two positions by a small spring (S); (c) a ratchet (R) which rides in the bottom of a trough beneath the above lever and extends from the head of the plunger to the barrel. One end of this ratchet is threaded for attachment with the plunger.

Part 2, the sandwich clasp (S.C.) embraces the head of the plunger and is attached to the threaded end of the ratchet by a hooked side extension.

Part 3, the wire rack (W.R.) is forked at one end to slip into the syringe holder, thereby fixing the entire instrument with adhesive tape or belting, or both, to the patient's thigh.

METHOD OF USE

The instrument is placed on a 5 cc., or preferably a 6 cc.* syringe and the syringe is filled with a solution of crystalline penicillin, streptomycin, or both. A curved plastic hub type needle is then attached and inserted into the anterior surface of the thigh, a few inches above the knee. A sponge, dipped in 70 per cent alcohol or 5 per cent ointment of sulfathiazole, is placed about the site of entrance of the needle and fastened with adhesive tape. The wire rack is placed on the "injector" and fastened with adhesive tape to the thigh. If desired, especially in male patients, an elastic belt may be used to hold the wire rack and instrument in position. To prevent accidental breakage of the syringe, a plastic cover is applied and held in place by the same belt (Figure 2).

After filling the instrument, a drop of sterile peanut oil is placed on the plunger, near its entrance into the barrel, to eliminate any possibility of "freezing" of the plunger when using solutions containing 500,000 units of penicillin or combinations of penicillin and streptomycin. To empty the syringe, the lever is tripped alternately, first on one end and then the other, permitting individual ½ cc. doses to be injected every two hours or at any interval desired.

PRELIMINARY STUDIES

Prior to the use of this instrument a study was made to determine whether penicillin would be destroyed by the heat of a patient's body when left in a syringe against the thigh. Eight 5 cc. syringes, each containing 200,000 units of penicillin, were strapped to the thighs of 8 patients. Four syringes contained amorphous penicillin and four contained crystalline penicillin in solution. After twelve and fourteen hours, respectively, the four syringes holding the two different types of penicillin were removed and penicillin levels determined.* The results showed no measurable destruction of either regular or crystalline penicillin.

Although no such study was made with streptomycin, the greater stability of this antibiotic drug indicates that its effect would not be altered by contact with the body for twenty-four hours.

Table 1 lists the disorders which have been treated with this new method during the past two years.

COMMENTS

Of more than 150 patients treated with penicillin and streptomycin during the past two years both at home and in the hospital, only 4 refused to continue treatment after the first twenty-four hours. Most of the patients treated were of the type found in the poorer districts of any large city. About 50 per cent of these were Negroes, and many were suffering from syphilis in its various stages. A few did not speak or understand English and 2 patients were blind. Never-

*Model 6 cc. syringes were supplied by the Premo Pharmaceutical Laboratories, Inc., New York, N. Y.

*Performed by Minerva Winokuv, B.A., under the supervision of David Merange, M.D., Mt. Sinai Hospital, Philadelphia.

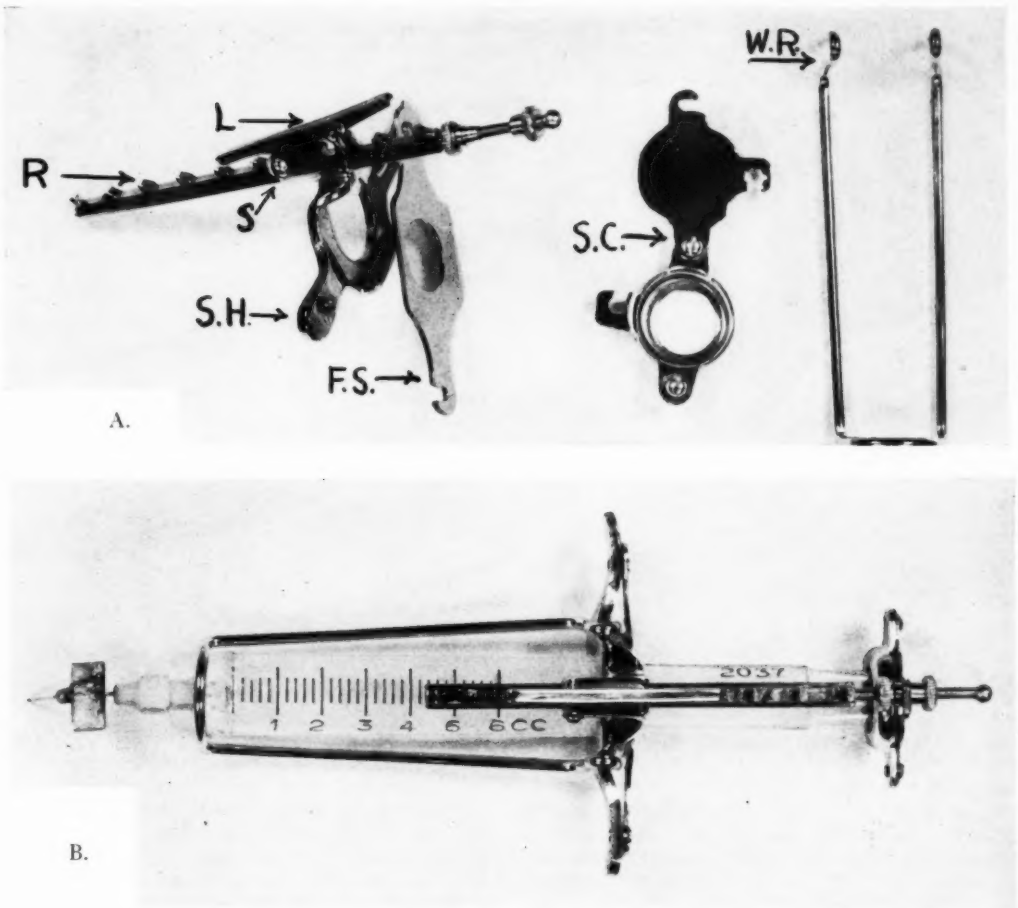

Figure 1. The Multidose Injector. A. Showing unassembled units: Part 1, syringe holder (S.H.); comprising a ratchet (R), lever (L), flat spring (F.S.), and spring (S). Part 2, sandwich clasp (S.C.). Part 3, wire rack (W.R.). B. Complete instrument with special 6 cc. syringe and needle.

theless, little difficulty was encountered in obtaining full cooperation in giving the injections every two hours as ordered.

The amount of aqueous penicillin administered daily varied from 200,000 to 500,000 units, depending on the nature and severity of the illness. Streptomycin was administered in doses of 1/12 gm. every two hours, a total of 1 gm. during each twenty-four-hour period. A number of patients who received penicillin therapy with the aid of this instrument in the Community Hospital in Philadelphia welcomed the absence of frequent skin punctures. It also lessened the demands on the already overtaxed nursing staff.

This new method of penicillin administration is applicable for the control of venereal diseases. In a few patients, acute pelvic inflammatory disease was quickly brought under control by penicillin after the sulfonamide drugs had failed. The method has been applied to approximately 50 patients with syphilis, some of whom were pregnant women. None of these patients failed to complete their course of therapy once it was begun.

Figure 2. Multidose Injector with constant indwelling needle. (Adhesive strapping not shown.) On alternate days the instrument was either reversed or transferred to the opposite thigh.

Recently some of the more robust patients, undergoing treatment for syphilis, had the penicillin-filled instrument strapped on daily to their thighs at the office; a plastic cover was applied, and the patient was sent home. The next day the patient removed the "injector" at home and after covering the site of the needle puncture with a sterile dressing, returned to the office for similar treatment. The busy physician, if he so desires, may request a nurse from the Visiting Nurse Society to apply the instrument in the patient's home. A few nurses have already been instructed in the use of this instrument.

DISADVANTAGES AND COMPLICATIONS

While there is necessarily some limitation of movement with the use of this instrument, many patients, with a low threshold of pain, carried on their usual household duties and even performed compensable work at home.

Only a few patients complained of disturbance of sleep by the presence of the instrument, and there was usually a member of the family who volunteered to give the injections during the night, in the home. The average individual quickly becomes accustomed to the presence of the instrument, as evidenced by its daily use for sixty consecutive days in two patients receiving streptomycin therapy.

In the treatment of many diseases, especially when improvement occurred, the patient was advised to take a double dose of penicillin at midnight and 4:00 A.M., thus constituting only a single disturbance during eight hours of sleep. Caronamide was occasionally given at these intervals to further insure high blood levels.

The temporary discomfort caused by the injection of streptomycin was much greater than that occurring with penicillin. However, in both instances and also with combined solutions, the residual tissue irritation, evidenced by local erythema and tenderness, quickly subsided within twenty-four hours.

Occasionally when patients were overactive, bleeding occurred and a drop of blood entered the barrel. Aside from causing blockage of the needle in rare instances, no harm was done.

At times when a needle was repeatedly used on a

TABLE 1

DISEASES TREATED WITH MULTIDOSE INJECTOR

PENICILLIN	STREPTOMYCIN*	COMBINED THERAPY**
Syphilis Primary Secondary Tertiary	Chronic cystitis (causative organism: proteus vulgaris)	Rectal abscess (recurrent)
Pneumonia	Chronic pyelonephrosis (causative organism: colon bacillus)	Chronic urethritis (Neisserian)
Breast abscess	Pulmonary tuberculosis	Bronchiectasis
Infections of the hand	Idiopathic pleurisy	Acute pyelonephrosis (resistant to penicillin therapy alone)
Acute inguinal lymphadenitis		
Peripheral infection		
Septic abortion		
Chronic osteomyelitis (recurrent)		
Migrant erysipelas		
Asthma (combined with penicillin aerosol)		
Bartholinian abscess		
Acute pelvic inflammatory disease		
Ulcer of leg, complicated by acute phlebitis		
Acute pyelonephrosis		

*Streptomycin used was in the form of streptomycin calcium chloride complex.

**1 gm. of streptomycin and 300,000 units of crystalline penicillin.

number of patients, blockage occurred. Usually this was overcome by simply advising the patient to press harder on the plunger.

One patient was sensitive to adhesive tape and developed a mild local reaction. This, however, did not necessitate discontinuation of therapy.

Some patients feared that the needle would break off beneath the skin. This actually occurred when conventional steel hub needles without a "security bead" were used; as a result, three broken needles had to be removed under fluoroscopy. With the use of plastic hub needles, there have been no breakages in more than 60 cases treated during ten months.

Allergic skin reactions were no greater than with any other method of aqueous penicillin administration. One technician, however, after working with penicillin and streptomycin for one year, developed a severe dermatitis of the hands.

Towards the end of the twenty-four hours of instillation of large dosages of crystalline penicillin, varying amounts of sediment often formed in the barrel of the syringe. These deposits did not cause any local irritation nor influence the beneficial results of penicillin therapy. The reason for these formations of sediment is being studied further. Peculiarly enough, when streptomycin and penicillin were combined in solution for simultaneous administration, no such sediment formed.

As with oral therapy, the accuracy of medication must depend on the patient, with this important difference: at the end of twenty-four hours the physician can easily determine whether all the medication has been injected.

ADVANTAGES

High dosages of aqueous penicillin can be administered at frequent intervals at home with resulting high blood levels similar to those obtained in the hospital.

No physician, trained nurse, or technician is required as a constant attendant for the administration of aqueous penicillin or streptomycin by this method. In seriously ill patients, a member of the family can give the injections without disturbing the patient during sleep, by merely reversing the position of the instrument on the thigh.

Only a single skin puncture is necessary for the twenty-four hours of penicillin or streptomycin therapy, thus requiring only a single daily visit by the physician or nurse.

Aside from the initial pain of the skin puncture

when the instrument is applied, the patients welcomed being spared the annoyance and discomfort of repeated injections with the conventional technic of parenteral therapy.

The majority of patients who had received repeated injections of penicillin every three hours and also by this new instrument preferred the latter method.

The combined administration of two or more antibiotics, because of the synergistic effect so necessary in illnesses due to mixed infections, is facilitated by means of this instrument.

With the use of crystalline penicillin, as well as streptomycin, there were no instances of fever, local necrosis, indurations, or phlebothrombosis.

For those patients receiving treatment at home, where some member of the family was acquainted with the technic of giving hypodermic injections, the instrument was filled with the antibiotic and if desired individual injections were given around the clock. A straight 25 gauge needle was then used, protected by a sterile 2-dram vial in the intervals. Thus no additional syringes had to be filled and preset dosages obviated any error.

The closed method of instillation of medicaments, as carried out with the Multidose Injector, prevents any loss of sterility and eliminates possible infections.

SUMMARY

1. A method for the administration of aqueous penicillin and streptomycin is described.

2. This new method for administration is applicable to patients who refuse hospitalization, ambulatory patients, those in the lower income group who cannot afford hospitalization, and those for whom hospital space is not available.

3. As the advantages of the synergistic action of combined antibiotic therapy are better realized, especially in the treatment of diseases of the chest and kidneys, any method which will facilitate their combined administration will be of greater value.

4. For physicians practicing in isolated communities and for those who, on occasion, must treat a stubborn patient who refuses hospitalization in spite of a serious illness, this new method of antibiotic administration may well prove to be a lifesaving measure.

5. In small hospitals, where the shortage of nurses is quite acute, this instrument enabling the convalescent or not too ill patient to take over the duty of frequent administration of antibiotics, will be a welcome aid to the hospital staff.

ADDENDUM

Since this paper was written approximately 50 additional patients have been treated with penicillin and 20 with streptomycin alone or combined in solution with penicillin. A few of the cases treated with streptomycin developed indurations which appeared to be of a toxic nature.

In order to reduce the frequency of visits one patient, under care for chronic cervical lymphadenitis with multiple draining sinuses, was treated with 2 gm. of dihydrostreptomycin administered in divided doses every four hours at one site. Toward the end of the fourth week hemorrhagic blebs developed at the site of needle punctures compelling a cessation of such therapy.

It therefore appears that the skin and immediate subcutaneous tissue can best tolerate 1 gm. of streptomycin at a single site.

A portion of the penicillin used in this study was supplied by the Division of Venereal Disease Control, Norman R. Ingraham, Jr., M.D., Chief, Department of Public Health, Philadelphia, Pa.

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Case Report

Anomalous Superior Thyroid Artery

A FINDING DURING RESECTION OF CAROTID BODY TUMOR

RICHARD B. CATTELL[1] AND E. S. PHILLIPS[2]

LAHEY CLINIC, BOSTON

THE SUPERIOR thyroid artery has a constant origin from the external carotid artery or from the anterior portion of the bifurcation of the common carotid. In over 100 ligations of the carotid vessels for intracranial aneurysm, Poppen found that the superior thyroid artery occasionally arose from just below the bifurcation but close to it. During operations for carotid body tumor the point of origin of the branches of the external carotid artery is important in establishing cleavage planes between the tumor and the main artery trunk. Experiences with the resection of carotid body tumors in the clinic have recently been reported by Drs. Lahey and Warren.* While exposing a large carotid body tumor we found an anomalous superior thyroid artery originating well below the bifurcation. The tumor was successfully resected, saving the common and internal carotid arteries and because of the rarity of the findings it seems worth while to record it.

All the standard texts and atlases of anatomy except one (Gray) describe and show that the superior thyroid artery arises from the anterior part of the external carotid or at the bifurcation of the common carotid artery. In a recent neck dissection for removal of a right carotid body tumor an unusual anomalous situation was encountered. A distance of 1.2 cm. caudal to its bifurcation into the external and internal carotids, the right common carotid gave off a large arterial trunk. After a course of 5 mm. this trunk divided into the superior laryngeal and superior thyroid arteries.

*LAHEY, F. H., and WARREN, K. W.: Tumors of the carotid body. Surg., Gynec. & Obst. 85:281-288 (September) 1947.

[1]Department of Surgery, The Lahey Clinic, Boston, Massachusetts.

[2]Fellow in Surgery, The Lahey Clinic, Boston, Massachusetts.

REPORT OF CASE

A white man, aged 41 years, came to the clinic September 26, 1947, with the chief complaint of a "lump in the right side of the neck." The lump which had gradually increased in size for three and one-half years of its known existence had grown at a more rapid rate the past six months. The subjective symptom in addition to the palpable mass was a sensation at times of pressure on his trachea accompanied by shortness of breath. No carotid sinus sensitivity could be demonstrated. Preoperatively, he could withstand but two minutes of complete compression of the right carotid artery. Compression of the common carotid was practiced six days without increasing tolerance.

The patient was operated on November 8, 1947, under endotracheal cyclopropane and ether anesthesia. The incision was made parallel with the anterior border of the right sternocleidomastoideus muscle which was retracted laterally. The carotid sheath was opened to allow dissection of the vessels above and below the tumor mass. Untied silk ligatures were placed about the common carotid below and the internal and external carotids above the tumor. As the mass was for the most part behind the vessels at the bifurcation area, the small amount of tumor overlying the arteries was split to free the arteries anteriorly. Then the external carotid artery was ligated with silk caudal to the origin of the single trunk for the facial and lingual arteries. Further dissection of the external carotid toward the bifurcation did not reveal the superior thyroid artery. It was then that the aforementioned trunk was found to arise 1.2 cm. caudal to the bifurcation from the anterior part of the common carotid artery.

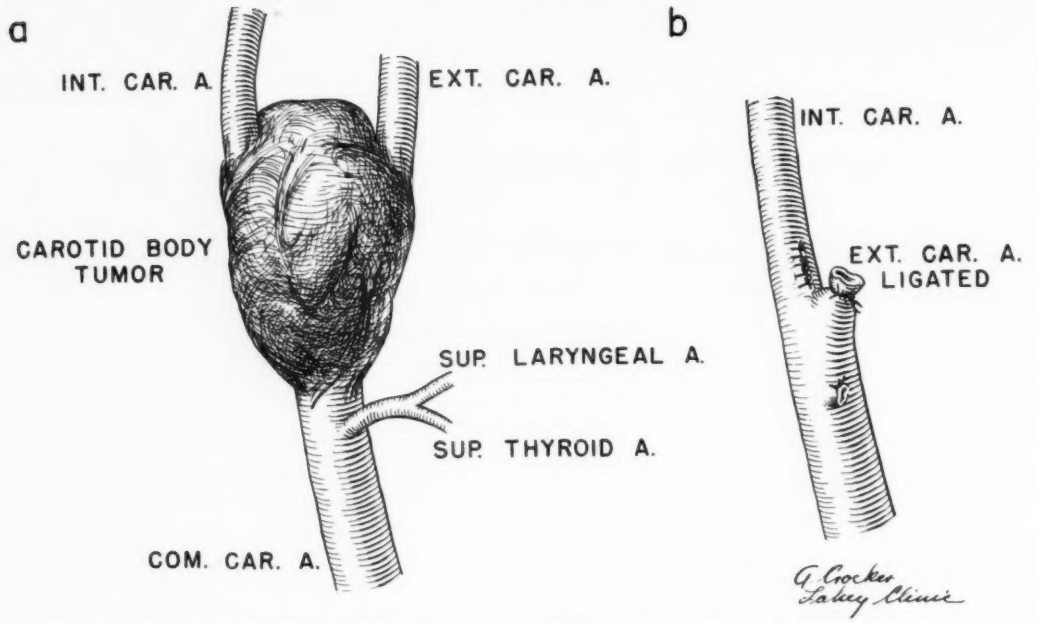


Figure 1*a*. Schematic drawing showing extent of carotid body tumor at the bifurcation and an anomalous superior thyroid artery coming off the common carotid artery. *b*. The condition of the carotid arteries after removal of a carotid body tumor. The external carotid artery and superior thyroid artery have been ligated and a rent in the internal carotid artery sutured.

As the tumor with the proximal end of the external carotid was being dissected from the common carotid, a rent appeared in the common carotid at its junction with the internal carotid. The force of the ensuing stream of blood enlarged the opening. The bleeding was controlled easily by a single tie in the previously placed sutures above and below the bleeding point. Then the slit which was approximately 1.25 cm. in the longitudinal axis of the vessel was sutured with a continuous through-and-through suture of silk (number 000000) on an atraumatic needle from above to below and then again from the caudal to the cephalad portion of the wound. While these stitches were being placed at intervals of two minutes the blood flow was allowed to be re-established for thirty seconds, avoiding hemorrhage by digital pressure on the rent. The suture which had effected an intima-to-intima approximation of the vessel wall controlled the hemorrhage effectively. Over this area was then placed a strip of saline moistened gelfoam. This was retained in position by two loosely tied plain catgut double zero sutures encircling both the artery and the gelfoam patch, producing approximation but no occlusion. Complete removal of the tumor was then effected.

The wound was closed without drainage. The silk ligatures on the common and internal carotid arteries were untied and allowed to remain *in situ* for emergency use, bringing them through the skin incision. Postoperatively, no anticoagulants were used but the patient was placed in an oxygen tent for twenty-four hours and kept in steep Trendelenburg position for seventy-two hours. As his convalescence was uneventful the ligatures about the arteries were removed on the seventh day and he was discharged on the tenth day.

Pathologic report—The mass consisted of tan to dark brown tissue weighing 15 gm. and measuring 4.5 cm. by 2.5 cm. by 2 cm., with firm fibrous strands traversing the surface which had a rubbery consistency on section. The microscopic diagnosis was carotid body tumor.

One month subsequent to operation the patient felt well, the wound healed, and there were no symptoms referable to carotid vessel disturbance.

Scientific Exhibit

Diabetes Mellitus

INTRODUCTION

THE DIABETES exhibit prepared by members of the George F. Baker Clinic and of the Metropolitan Life Insurance Company for the annual meeting of the American Medical Association at Atlantic City in June 1947, revealed advances in our understanding of many aspects of diabetes and its complications. Further evidence of the magnitude of the diabetic problem has been brought forward by the demonstration of the high incidence of diabetes found in a survey of the population of Oxford, Massachusetts, by the United States Public Health Service. Not only the large number but also increasing duration of life of diabetic patients affect the size of the problem. Thus, the expectation of the life for diabetics of all ages, but particularly the diabetic child has again increased materially. Improvements in the treatment of coma, pregnancy and surgical complications have been outstanding features. Notable advances in the experimental study of diabetes were summarized in two placards contributed by Dr. Francis D. W. Lukens. Complying with the request of the Editor of *Postgraduate Medicine* we have reassembled our charts and with a few minor changes present them as representing features of diabetes important for consideration today.

ELLIOTT P. JOSLIN

In association with Howard F. Root, Priscilla White, Alexander Marble, Allen P. Joslin, C. Cabell Bailey and Herbert H. Marks

JUVENILE DIABETES AND ITS COMPLICATIONS

COMPLICATIONS

If coma is used as an index of control of diabetes, the frequency and extent of arteriosclerosis parallel its occurrence. In the 15 cases without vascular disease, incidence of coma was but 13 per cent. Fifty per cent of the patients with demonstrable but not incapacitating vascular disease had had coma. Seventy-five per cent of 46 cases with severe vascular lesions had survived at least one attack of diabetic coma.

Hopeful is the fact that diabetes is known to have existed in two juveniles for more than 25 years and the roentgenologist, the ophthalmologist, and internists could find no evidence of lesions. Fifteen have survived twenty years and have similarly been found free from vascular disease. Control of diabetes was in general better in this group.

HOPE FOR DIABETIC CHILDREN

Anyone who has treated diabetic children for forty-nine years has experienced poignant reactions when compiling the results obtained. Here and there years ago there was a ray of hope for diabetic children, because some special case would live a few years longer than another. The reason therefore was usually misinterpreted, but the fact remained.

Known Complications in 308 Diabetic Children Surviving More Than 20 Years

COMPLICATION	INCIDENCE Per Cent
Epilepsy	3
Tuberculosis	4
Skin Lesions	5
Cataract	6
Retinitis Proliferans	6
Pyelonephritis	13
Dwarfism	15
Hepatomegaly	16
Neuropathies	21
Infantilism	23
Skin Infection	30
Albuminuria	34
Hypertension	40
Coma	40
Retinal Hemorrhage	70
Arteriosclerosis	80

COMA—THE BEST INDEX OF POOR CONTROL OF DIABETES

INCIDENCE OF COMA IN 111 JUVENILES
STUDIED FOR ARTERIOSCLEROSIS AFTER 20 YEARS OF DIABETES

Arteriosclerosis	Cases No.	Coma Per Cent
None	15	13
Demonstrable	50	50
Incapacitating	46	75

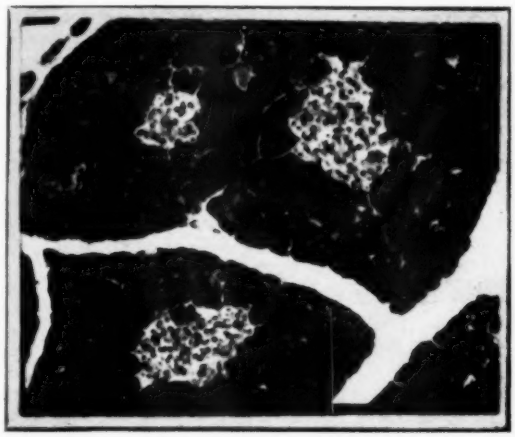
SUGGESTED PROGRAM FOR PREVENTION OF VASCULAR DISEASE

1. Control the diabetes
2. Correct all abnormalities

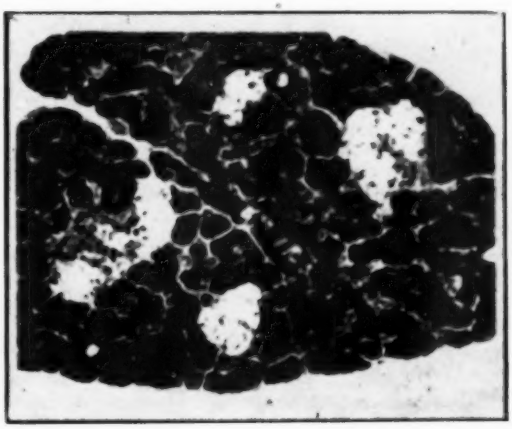
DIABETES PRODUCED EXPERIMENTALLY

By (1) Pancreatectomy; (2) Anterior Pituitary Extract; (3) Alloxan; (4) Glucose Administration (prolonged)

Island cell damage follows hyperglycemia produced by: (1) overfeeding to partially depancreatized animals; (2) pituitary extract; (3) glucose administration.



Pancreas of normal cat showing islands of Langerhans. x240.

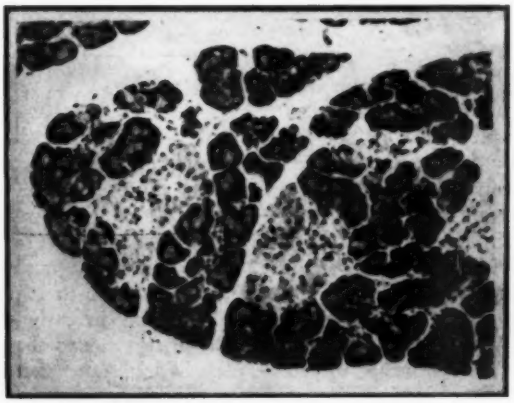


DIABETIC CAT R-3—Biopsy of pancreatic remnant after 2½ months of glycosuria and before insulin treatment. Islands are large and numerous but show marked hydropic degeneration. By the Bensley-Mallory stain, remaining cells have been identified as alpha cells; normal beta cells rare or absent.

If Hyperglycemia Continues, Irreversible Atrophy of Islands Results

Pancreas of cat showing atrophy of islands of Langerhans after 190 days of diabetes. This lesion is irreversible.

In early stages if hyperglycemia is prevented by (1) low diet, (2) insulin, (3) phloridzin, **restoration of islands occurs**



DIABETIC CAT R3—Biopsy of pancreatic remnant 66 days after the end of insulin treatment. The islands are normal in appearance.

DIET AND INSULIN

Control of Diabetes Requires the Normal Utilization of a Diet Adequate Not Only in Carbohydrate, Protein and Fat, But Also in Vitamins and Minerals

SAMPLE DIET

Carb. 168, Protein 85, Fat 98, Cal. 1894

	Breakfast		Dinner		Supper	
Food	Grams	Portion	Grams	Portion	Grams	Portion
Eggs		1				
Meat			75	Medium	75	Medium
Bacon	15	2 Strips				
Orange	100	Small	150	Medium	150	Medium
Oatmeal	15	½ Cup				
5% Veg.			150	1 Cup	150	1 Cup
10% Veg.			75	½ Cup	75	½ Cup
Potato					90	Medium
Butter	10	2 Teasp.	10	2 Teasp.	10	2 Teasp.
Cream	60	2 Ounces	30	1 Ounce	30	1 Ounce
Milk	120	½ Cup				
Bread	30	1 Slice	30	1 Slice	30	1 Slice

Bedtime — 2 Uneedas + 120 Milk *Substitution Lists are Used to Allow Variety*

USE INSULIN PROMPTLY

To Promote Utilization of Food, to Correct Fluid and Mineral Balance and to Correct or Prevent Acidosis

Insulin Requirements in 813 Consecutive Diabetic Patients in New England Deaconess Hospital

Age of Admission	Total Admissions	Sex M	Sex F	Duration Diabetes	Carb. at Discharge	None	Insulin CI	Insulin PZI	Insulin CI & PZI
0-14	47	30	17	3.3	179				47 (12 + 24)
15-24	75	23	52	9.7	185	1		4 (39)	70 (21 + 45)
25-54	320	129	191	11.1	169	30	53[3]	77 (19)	210 (13 + 36)
55-Over	371	159	212	12.3	158	33		203 (16)	135 (11 + 32)
Totals and Averages	813	341	472	10.3	166	64	53[3]	284 (19)	462 (14 + 35)

Compared with a survey of 1831 admissions in 1941, the average duration of diabetes has risen from 7.6 to 10.6 years, the carbohydrate at discharge from 162 to 166 grams, but the total insulin remains the same.

The triad of diet, insulin, and exercise makes up the foundation for treatment of diabetes. The basic diet should be simple and easily understood both by the patient and the physician. Such a basic diet may be amplified and varied according to the different occupations and the caloric needs of the individual. The contents of most diabetic diets are within the following limits: carbohydrate 150 to 225 gm., protein 70 to 120 gm., and fat 60 to 125 gm. Frequently it is desirable to divide the carbohydrate food in the diet so that in addition to the 3 regular meals, 10 gm. of carbohydrate are taken in the midmorning, midafteroon and perhaps 15 gm. of carbohydrate on retiring.

The amount of exercise or physical work required by a patient's occupation must be carefully considered in planning the diet. Patients need special instructions to take extra carbohydrate in the event of unusual exercise or work.

Protamine zinc insulin should be considered the insulin of choice for most patients because of its prolonged action. Indeed among 813 diabetic patients recently treated at the Deaconess Hospital, a total of 284 patients were controlled with protamine zinc insulin only. Of these 813 patients, 203 were 55 years of age or older. In the younger group of patients, combinations of crystalline insulin (CI) and protamine zinc insulin (PZI) were required and the average dose for 462 patients was 14 units of crystalline and 35 units of protamine zinc insulin. Sixty-four patients required no insulin.

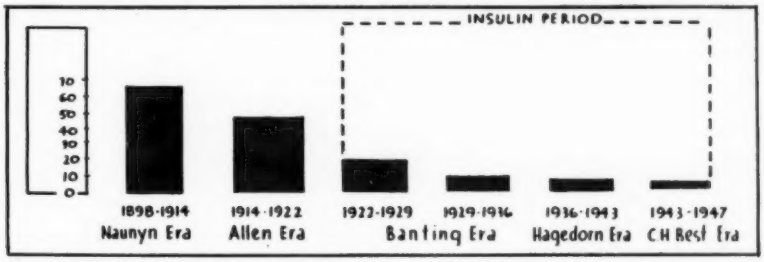
COMA—AN EMERGENCY DUE TO LACK OF INSULIN

IMPROVEMENT IN TREATMENT

George F. Baker Clinic

Decline in Percentage of Coma Deaths Among 9091 Fatal Cases

(Through May 12, 1947)



Compiled by the Statistical Department of the Metropolitan Life Insurance Company

COMA PREVENTED BY EDUCATION OF PATIENTS CURED BY EARLY AND LIBERAL USE OF INSULIN

DECLINE IN MORTALITY OF 677 CASES TREATED AT NEW ENGLAND DEACONESS HOSPITAL

	1923-1940		1940-Jan. 1, 1947
Cases	478		199
Deaths (percentage)	12%		1.5%
Insulin given in first	1923-1927	1932-1933	1942-1947
3 hours (units)	83	136	206
Mortality	18%	11%	1.5%

MENTAL STATE AND MORTALITY IN COMA

	1923-1939		1940-1947	
	Cases	Mortality	Cases	Mortality
Mental Condition	No.	Per Cent	No.	Per Cent
Conscious	187	3.2	39	2.5
Semi-conscious	182	8.8	130	0.7
Unconscious	83	35.0	42	9.4
Totals and Averages	452	11.2	211	2.7

PROGNOSIS RARELY HOPELESS, IF SUFFICIENT INSULIN IS PROMPTLY GIVEN

DIABETIC COMA

Deaths from coma are needless. The education of patients should emphasize necessity for the early reporting of symptoms such as nausea, vomiting, and pain in the abdomen, to the family physician. In the actual treatment of coma, early diagnosis and the liberal use of insulin in the *first three* hours of treatment have seemed to be responsible for spectacular improvement in results of treatment.

The outlook for coma cases depends upon the degree and duration of unconsciousness. The mortality is low in those patients where acidosis has not as yet resulted in complete unconsciousness. In 83 patients totally unconscious, the mortality in the earlier period between 1923 and 1939 was 35 per cent. More recently, however, in a series of 42 cases the mortality in totally unconscious cases has fallen to 9.4 per cent. Again we are convinced that this change in the results of treatment is due chiefly to the use of larger doses of insulin in the first three hours of treatment.

JUVENILE DIABETES

The management of severe diabetes in children presupposes continuous substitutional insulin therapy, regular and protamine, the former correcting day and the latter night hyperglycemia. Age rather than the degree of glycosuria is the best guide for the initial prescription of insulin—10 units for the total dose for children under 5 years of age, 20 units for those between 5 and 10 years, 30 for those over 10. Young children require more of the rapidly than of the slowly-acting insulin when given as separate injections. At age 5, the requirement is equal for both, and older children require more, nearly twice as much, slowly than rapidly-acting insulin. Readjustments of insulin are made according to pre-meal urine tests.

The potentiality for growth in juvenile diabetes is good. The diabetic child at onset of diabetes is typically tall with advanced bone and dental development. Modern therapy favors continuation of the superior level. In the remote past growth failures occurred. Correction with diet alone does not appear to be adequate. Failures of growth respond to sex endocrine therapy, testosterone, chorionic gonadotropin, estrogen, thyroid, all of which are also effective in developmental failures.

Reproduction of living children in the past has been difficult for young diabetic women. Only 1 pregnancy in 2 resulted in a living child. Today, limited only by advanced vascular disease, the chances for survival are 9 out of 10.

Coma, tuberculosis, and sepsis, the chief complications of the diabetic child up to 1940, have been largely conquered, leaving vascular disease the enemy of the young diabetic surviving 15 years. A program for correction of all abnormalities: application of the findings of the experimentalists; more rigid control of diabetes must be adopted in the hope of protecting the future generation of diabetic children against the destructive ravages of vascular disease.

In Addition to Combating All Difficulties of Adult Diabetic Life
the Child Must Solve Six Problems

PROBLEMS

Management of Severer Diabetes	Establishment of Economic Security
Attainment of Normal Growth	Reproduction of Living Healthy Children
Completion of Development	Survival 3 Times as Long as an Adult

SOLUTION

Management

Insulin—continuously

Types—RI for day
PZI for night

Dosage at onset of diabetes

Age Yrs.	Total Units	Ratio Units RI:PZI
1-4	10	2:1
5-9	20	1:1
10-14	30	1:2

Growth and Development

Calories Adequate
Proportions Favorable
Utilization Perfect

1000 calories at age one
Add 100 calories each year of age

	Per Cent Calories
Carbohydrate	40
Protein	20
Fat	40

Glycosuria minimal

Correct dwarfism and infantilism
Male: Rx, Testosterone, chorionic gonadotropin, thyroid
Female: Rx, Thyroid, estrogen

Employment

(308 children surviving 20 years)
Gainfully employed = 90%

Reproduction

	Per Cent
Maternal survival assured	100
Total fetal survival	90

SURVIVAL

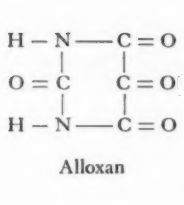
COMA, SEPSIS, TUBERCULOSIS PREVENTABLE

Vascular disease (nephritis) remains chief enemy of young diabetic surviving 15 years.

Eliminate vascular disease by:
a. Control of diabetes
b. Correction of all abnormalities

ALLOXAN DIABETES

A Single Injection of Alloxan Destroys the Beta Cells of the Pancreatic Islets of Langerhans and Produces Diabetes

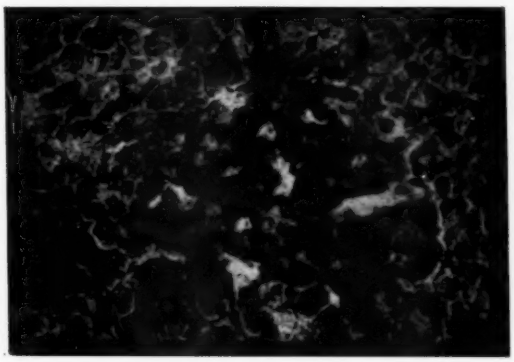


Alloxan

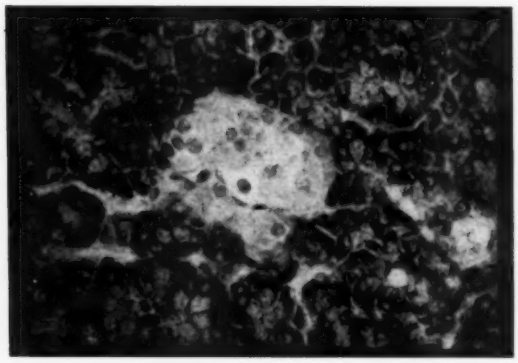
DIABETOGENIC DOSE

	Mgs. Per Kg.	
Rabbits	150-200	Intravenously
Rats	150-200	Subcutaneously
Dogs	50-75	Intravenously
Monkeys	300	Intravenously
Pigeons	125-200	Intravenously
Cats	1000	Orally
Turtles	400	Intrapulmonarily
Sheep	90	Intravenously

Pathology: Early Degenerative Changes Can Be Seen in the Insulin-Forming Beta Cells 5 Minutes After Alloxan Is Injected—Only Alpha Cells Remain in 24 Hours



Normal Islets of Langerhans



5 weeks after Alloxan—Largely Alpha Cells, few degenerating Beta Cells

ALLOXAN IN HUMANS

Several Reports Suggest:

1. Alloxan can produce islet destruction and diabetes.
2. Alloxan may produce severe injury including liver necrosis and death.
3. Islet cell adenoma or carcinoma are resistant to alloxan—more so than normal islet cells.

ALLOXAN—MECHANISM OF ACTION UNCERTAIN

1. Alloxan has a strong affinity for sulfhydryl compounds.
2. Injection of large doses of sulfhydryl compounds (cysteine or glutathione) preceding the injection of alloxan prevents diabetes.
3. Many enzymes contain sulfhydryl radicals including the important carbohydrate enzyme hexokinase.
4. Alloxan possibly destroys the pancreatic islets by enzyme inactivation.

RECENT ADVANCES IN EXPERIMENTAL DIABETES

I. Sustained Hyperglycemia Caused by the Prolonged Administration of Glucose Results in Permanent Diabetes

(LUKENS and DOHAN)

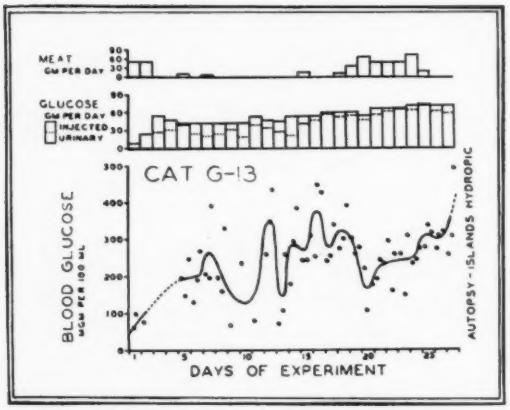


Fig. 1. Cat G-13 was given intraperitoneal injections of 20% glucose at approximately 8-hour intervals. Upper portion shows anorexia caused by injections. Middle portion gives daily doses of glucose and glycosuria. In the lower portion, the curved line shows the daily average of the blood sugars (dots). After fluctuating widely for the first two weeks, hyperglycemia was established for the last two weeks.

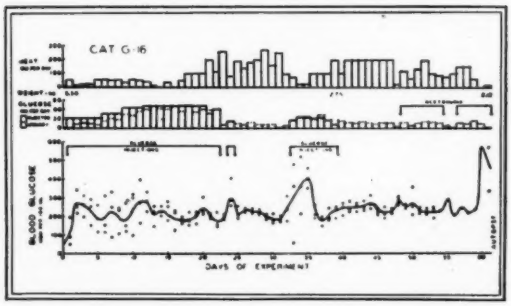


Fig. 2. Permanent diabetes induced by injections of glucose. Glucose was given with some interruptions for 39 days during which hyperglycemia was maintained. After stopping glucose the cat remained diabetic. It developed acetonuria and died in coma with a CO_2 of 11 vols. %.

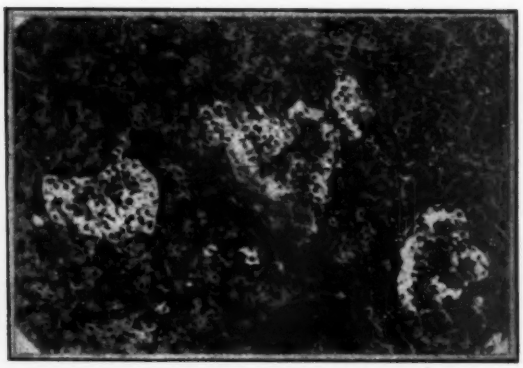


Fig. 3. Low power photograph of pancreas of cat G-13 (Fig. 1) showing hydropic degeneration of beta cells. Bensley-Mallory stains showed that the cells that remained were chiefly alpha cells.

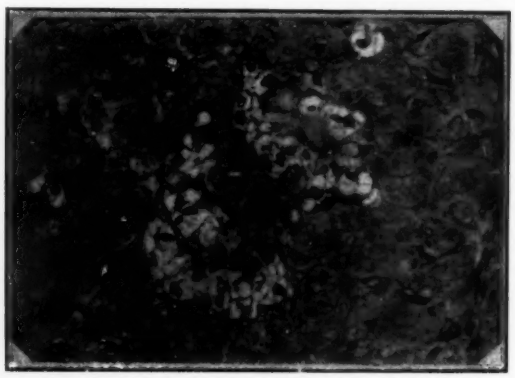


Fig. 4. High power view of island of Langerhans of cat G-13 (Fig. 1).

Fetal conditions were three: (1) intrauterine deaths, (2) congenital defects, and (3) atelectasis.

Sex hormonal imbalance appeared to be the most important single harmful factor. Measured by chorionic gonadotropin and pregnandiol levels when it was abnormal, as it was in 62 cases, the fetal survival was 44 per cent; when abnormal and corrected, as it was in 218 cases, 90 per cent; when normal (72 cases) 97 per cent.

Drainage, suction, oxygen and dehydration constitute our neonatal program for the infant.

An unfavorable outcome depends upon gross congenital defects of the infant, advanced vascular disease of the mother. If the pelvic arteries are calcified, the chances of the fetus surviving with programs outlined fall from 90 to 30 per cent.

PREGNANCY

Fetal Mortality Is the Problem of Obstetrical Diabetes
352 Infants Born to 350 Diabetics
1936 — 1947

	Per Cent		Per Cent
FETAL MORTALITY	16	MATERNAL MORTALITY	0.3

CONDITIONS ASSOCIATED WITH 60 FETAL DEATHS

		Number
MATERNAL	Hypoglycemia	0
	Sepsis	1
	Coma	5
	Vascular Disease	8
	Sex Hormonal Imbalance	58
FETAL	Congenital Defects	3

SEX HORMONAL BALANCE PARALLELS FETAL SURVIVAL

Abnormal (62) Cases	Abnormal Corrected (218) Cases	Normal (72) Cases
44 Per Cent	90 Per Cent	97 Per Cent

FAVOR FETAL SURVIVAL BY

1. Control of maternal diabetes
2. Early timing of delivery
3. Correction of disturbed chemistry
   a. Low salt high protein diets
   b. Ammonium chloride—4 to 8 gm. daily
   c. Estrogen and progesterone: daily intramuscular injections

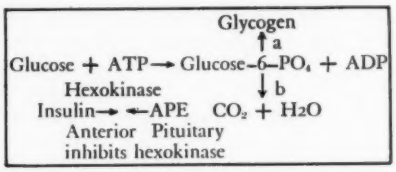
Example: Weeks of Preg.	Stilbesterol mg.	Proluton mg.
6 to 19	5	5
20 to 23	10	10
24 to 27	20	20
28 to 31	30	30
32 to 38	40 to 100	40 to 100

4. Management of infant
   a. Drainage
   b. Suction
   c. Oxygen
   d. Dehydration

II. The Hexokinase Reaction (Cori *et al*). Anterior Pituitary Inhibits the Utilization of Glucose. Insulin Prevents This Inhibition.

Cori (Harvey Lect.-1946) has described the following action of insulin, demonstrable in a cell-free enzyme system.

Fig. 5



Legend: ATP-adenosine triphosphate
ADP-adenosine diphosphate
Intermediate steps at a and b have been omitted.
The *enzyme hexokinase* is present in liver, muscle, brain and probably all tissues.
The *anterior pituitary* may be added as extract. It is present in extracts of diabetic tissues.

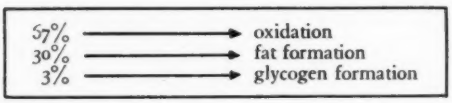
Adrenal cortical extracts do not act alone but enforce the inhibition when pituitary hormones are present.

Insulin alone has no effect on hexokinase reaction, but releases the reaction from pituitary inhibition.

III. Fat-Forming Action of Insulin (Stetten)

Quantities Involved in Various Pathways (Stetten)

In rats fed a maintenance diet, studies with isotopes indicate this disposition of the ingested carbohydrate.



EXPERIMENTAL DIABETES

Despite the enforced interruption due to World War II, important studies in carbohydrate metabolism and the pathogenesis of diabetes have been carried out in many laboratories. Three lines of approach illustrated on the accompanying charts are of especial interest.

Dohan and Lukens reported that the prolonged administration of glucose parenterally to normal or partially depancreatized cats causes permanent diabetes. (See Figure 2 on page 2.) The importance of this discovery etiologically is self evident, but is surpassed by its therapeutic implications. If hyperglycemia will cause diabetes in an animal with an undamaged pancreas, consider what it might do to an animal whose pancreas was already damaged.

From Cori's laboratory (Harvey Lectures, 1946) have come reports of studies of fundamental and far-reaching significance. Briefly, the work of Cori and associates indicates that at least one of the sites of action of insulin is at that stage of intermediary carbohydrate metabolism at which glucose is transformed into glucose-6-phosphate with the aid of adenosine triphosphate and under the influence of the ubiquitous sulfhydryl enzyme, hexokinase. Glucose, in itself metabolically inert, is thus admitted to the metabolic system. Cori's findings indicate that *in vivo* or *in vitro* anterior pituitary extract inhibits the action of hexokinase. Insulin alone has no effect on the hexokinase reaction, but releases it from anterior pituitary inhibition.

Using radioactive isotopes, the newly found tools of metabolic research, Stetten has acquired a great many valuable data. Of particular interest is the fact that, in rats fed a maintenance diet, the formation of fat following the ingestion of carbohydrate accounts for 10 times as much of the fed material as does glycogen (30 per cent as opposed to 3 per cent).

In 1889 von Mering and Minkowski announced that diabetes followed removal of the pancreas in dogs. Sustained hyperglycemia is the one feature common to the overfeeding of partially depancreatized animals, the injection of pituitary extract, and the prolonged administration of glucose. It is the prolonged elevation of the blood sugar which, through overwork, causes islet cell exhaustion and damage with resultant diabetes.

In the early stages of the development of experimental diabetes of the types named, if hyperglycemia is prevented by a low diet, insulin or phloridzin, restoration of normal islet structure occurs and diabetes is "cured" or prevented. If, however, the early stage of hydropic degeneration is passed and atrophy of the islets has occurred, the process is irreversible.

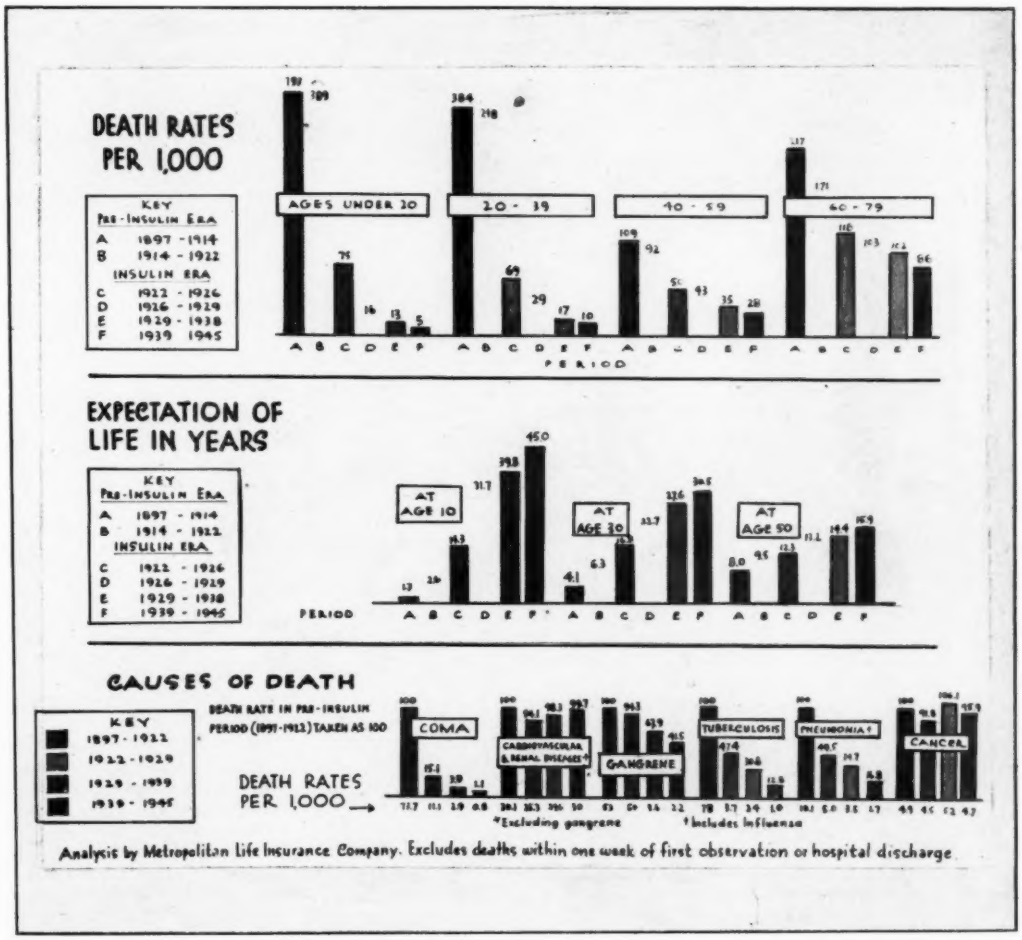
These findings have a direct application in the treatment of human patients. They suggest that (1) hyperglycemia is ***not*** harmless as it is an indication of poorly controlled diabetes; (2) overnutrition should be avoided; (3) adequate insulin therapy is essential if hyperglycemia cannot be controlled with diet alone; (4) a ray of hope for the prevention and possible cure of diabetes is given.

PROGNOSIS IN DIABETES

What pleases us most of all in the outlook for our patients is the fact that for each period and for each age group there has been a fall in death rates per 1000. Thus there is no age in which a diabetic acquires the disease, but what we can say to him that danger of death is decreasing and the prospect for life is improving.

The changes in the causes of death show almost complete elimination of diabetic coma from among these patients. There has been an increase of cardiovascular-renal disease and cancer, in part due to the longer duration of the diabetes and the older age of the patients at death. Yet even here there is more than a ray of hope, because in arteriosclerosis of the lower extremities, characterized by gangrene, the death rate has dropped from 58 per cent since insulin came into use. Now the problem is to lower the death rates for arteriosclerosis in the brain, heart and kidneys.

The reductions in the death rates from tuberculosis and from pneumonia are beginning to approximate the decline in deaths from coma.

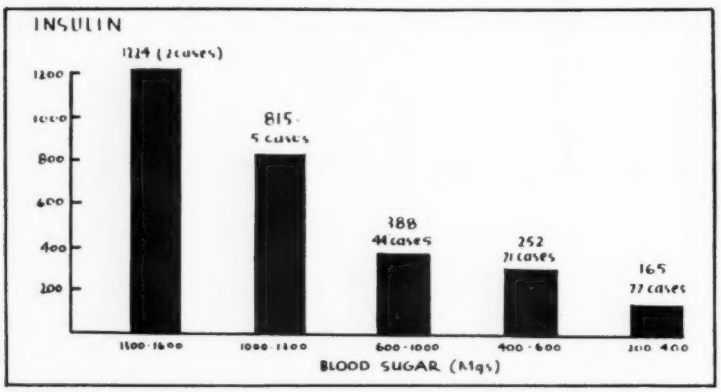


TREATMENT OF COMA

The treatment of advanced coma depends primarily upon the correct estimation and prompt administration of an adequate dose of insulin. Without supportive laboratory studies treatment will be delayed. Therefore suspected coma cases should be transferred to a hospital. As soon as the diagnosis of diabetic coma is evident from physical examination and tests of the urine, insulin should be given immediately in doses which may vary within a wide range. A patient with diabetes long under treatment who is entirely unconscious may need 200 to 500 units in the first three hours of treatment. A small child with diabetes of recent onset may require only 30 to 50 units.

In addition to the use of insulin the treatment of the accompanying dehydration and shock is essential. The administration of normal saline solution intravenously and subcutaneously should be begun immediately after admission in those patients where dehydration is extreme. A rate of fluid administration may be as great as 1000 cc. per hour until 5000 cc. are given. When anuria is threatening as indicated by a disappearance of acetone bodies and a decline in urine production, the administration of salt solution may be continued until an amount equivalent to 10 or even 15 per cent of the body weight has been given. Gastric lavage should always be carried out in coma cases. When the blood sugar has begun to fall, it is evident that sufficient insulin has been given and then the administration of food by mouth or by vein is important. Ten grams of carbohydrate per hour is a safe rate. No glucose solution is needed in the first six hours of coma treatment.

Prognosis Depends Upon Treatment Given in the First Six Hours—Improvement in Our Treatment Is Due to More Insulin in the First Three Hours



BLOOD SUGAR LEVEL CORRELATED WITH INSULIN DOSE IN 199 CASES DIABETIC COMA

Oct. 1940 — Jan. 1, 1947

CO_2 under 9 m. eq.; fatalities 3

PRINCIPLES OF TREATMENT

1. Hospitalize suspected coma patients for diagnosis. If necessary, catheterize for urinalysis. Verify diagnosis by blood sugar and CO_2 tests within the hour.
2. Insulin immediately upon diagnosis in dosage 50-500 units in first 3 hours, according to duration and severity of coma, age of patient and previous treatment. Insulin resistance increases as acidosis advances. Give insulin sufficient to produce rapid decline in blood sugar in first few hours.
3. Treat hyperglycemia vigorously and thus avoid damage to islands of Langerhans (Lukens).
4. Normal saline intravenously and subcutaneously 2000-5000 cc. in 12 hours or in extreme dehydration with anuria up to 10 per cent of body weight.
5. Gastric lavage.
6. Enema. Keep patient warm, but avoid burns.
7. When falling blood sugar indicates desired insulin effect and stomach tolerant, give fluids by mouth 100-200 cc. hourly of broth, gingerale, orange juice or oatmeal gruel. Aim at 10 gm. carbohydrate per hour. For persistent unconsciousness or recurrent vomiting, intravenous feeding may be necessary.
8. Give no glucose in the first 6 hours. (a) Blood and body fluid already contain excessive glucose utilizable only if sufficient insulin is given. (b) Added glucose may precipitate renal block and anuria. (c) Glucose given in amounts exceeding caloric needs may be converted to fat rather than oxidized. (d) The value of repeated blood sugar tests as guide to treatment is lost. (e) Loss of potassium from blood and tissue cells with resulting paralysis of voluntary muscles may follow excessive glucose administration. (f) Insulin requirement is increased.

SURGERY

The great prolongation of life made possible by the use of insulin brings many more diabetics into later decades of life where surgical complications are more frequent. Where formerly the hazard of surgery was so great that operative treatment was usually postponed or avoided, now, thanks to the better control of diabetes and improvement in surgical management, surgery is done as necessary and the mortality rate is extraordinarily low. Probably at some time nearly 50 per cent of all diabetic patients will need some type of surgical treatment.

In many diabetic patients with infections of long standing, malnutrition and emaciation with resulting anemia and hypoproteinemia are present. If acidosis has complicated the infection, dehydration may be extreme.

The administration of vitamins intravenously and whole blood transfusions may be generously employed. Most important has been the control of infection by the use of the new chemotherapeutic substances, the sulfonamides, penicillin, and streptomycin. In the infections of the extremities the administration of penicillin in liberal amounts, 300,000 to 500,000 units daily prior to operation, and for some days after operation, is almost routine.

Gangrene still presents the major surgical complication in older diabetic patients. The most significant advance in surgery of the extremities in recent years has been the use of the transmetatarsal amputation for patients with gangrene or osteomyelitis involving one or more toes. This has made possible the avoidance of thigh amputation and the preservation of a useful foot. The surgical judgment and experience of our colleagues has made possible the selection of those patients where the blood supply, although seriously impaired, still permitted healing in all but 16 of 111 transmetatarsal amputations.

Control Diabetes with Diet and Insulin; Deliberate Preparation Rather Than Emergency Surgery; Early Mobilization

Secure proper fluid balance. Utilize parenteral feedings in malnutrition, anemia and hypoproteinemia, including vitamins and whole blood. Chemotherapy.

DECREASED OPERATIVE MORTALITY

Period	Total Operations No.	Death Per Cent
1923-1941	3551	7.3
1942-1947	1736	2.7

DECLINE IN MORTALITY FROM GANGRENE AND COMA AS DIABETIC TREATMENT IMPROVES

	Deaths			
	Number	Duration Diabetes Yrs.	Causes of Death Gangrene Per Cent	Coma Per Cent
1922-1929	1448	8.1	8.5	15
1930-1936	2130	11.1	7.9	5
1937-1943	2583	12.9	5.1	3.4
1944-1946	651	14.1	2.9	3.1

GANGRENE—*Common in mild but uncontrolled or neglected diabetes, usually of long duration and in the obese.*

111 TRANSMETATARSAL AMPUTATIONS

Age Yrs.	Cases No.	One Fatality Healed Successfully No.	Per Cent	Higher Amputation Subsequently No.	Duration Diabetes Yrs.
40-49	5	5	100	0	15
50-59	34	30	91	4	10
60-69	48	39	81	9	12
70-79	22	19	86	3	13
80-	2	2	100	0	1

PREVENTION—*Treat incipient diabetes aggressively. Each danger of trauma, blisters, burns and use of strong antiseptics.*

ALLOXAN DIABETES

Alloxan is a pyrimidine related to and obtainable from uric acid. Alloxan, when injected into animals, causes diabetes by producing a selective destruction of the beta cells in the islets of Langerhans in the pancreas. Alloxan is stable only in acid media. Neutralized alloxan is not diabetogenic.

Lazarow found that the administration of certain sulfhydryl compounds, glutathione, cysteine, or thioglycolic acid, immediately before injection of alloxan prevents the development of diabetes. Since alloxan reacts readily with the sulfhydryl group it is quite probable that the sulfhydryl compounds join with alloxan, inactivating or destroying the alloxan before it reaches the pancreas. There is a marked decrease in blood glutathione in rabbits following the injection of alloxan.

Since alloxan destroys pancreatic islet cells its use in the treatment of islet cell tumors was immediately suggested. Brunschwig *et al* first used alloxan in a human with an islet cell tumor but obtained only transitory improvement. Although Talbot and Bailey obtained encouraging results in a nine-month-old baby with hyperinsulinism by using repeated small daily doses of alloxan, further reports suggest that islet cell tumors are more resistant to alloxan than are normal islet cells and the toxicity of alloxan is so great that acute liver necrosis and death may follow its use in humans. Conn reported definite diabetes in one human following the injection of alloxan thus showing that alloxan may be diabetogenic for humans as well as for animals.

EXPECTATION OF LIFE

For White Persons in the General Population and for Diabetics of the George F. Baker Clinic

Age	United States 1939-1941	Diabetics 1939-1946
10	58.9	45.0
20	49.6	37.3
30	40.5	30.5
40	31.6	23.0
50	23.3	15.9
60	16.0	10.6

The expectation of life of diabetics is continuing to increase at every age. The differences between the tables prepared by the Metropolitan Life Insurance Company from records of the George F. Baker Clinic for the periods of 1929 to 1938 and 1939 to 1945 are striking. Whereas in the former table the life expectancy of diabetics was approximately two-thirds, in this recently compiled table the life expectancy has risen to about three-fourths that of the general population. Specifically the expectancy has advanced at successive ten-year age intervals beginning with the age of 10 years, by 5, 4, 2½, 2, 1.9 and 0.6 years respectively.

The Medical Bookman

ABDOMINAL OPERATIONS*

This comprehensive work on "Abdominal Operations" by Rodney Maingot should, as the author intended, appeal to those engaged in the practice of general and abdominal surgery and those engaged in residencies in surgery. It is an extremely practical and very readable comprehensive study of abdominal surgical conditions.

The book is divided into eleven parts, each dealing with the major organs of the abdominal cavity. Difficulties and dangers, pre- and postoperative care, immediate and late results, clinical and pathologic aspects, are all stressed, as well as various technics and operative measures.

The first section deals with stomach and duodenum and covers the various surgical technics and their indications. That portion concerned with vagotomy, transthoracic and transabdominal, has been contributed by Dragstedt and emphasizes that benign peptic ulcer, be it gastric, duodenal, or gastrojejunal, can be expected to heal following complete vagotomy. In gastric ulcer, the question of the ulcer's being malignant is ever present and when there is the slightest doubt as to the nature of the lesion, gastric resection should be carried out in preference to vagotomy.

Duodenal ulcer is thoroughly discussed and the author feels that, at the present time, the choice of surgery for duodenal ulcer lies between gastrojejunostomy and gastric resection, with or without vagotomy. The author prefers the anterior or posterior Polya type of subtotal gastrectomy (favoring Bancroft's method) in cases of so-called irremovable duodenal ulcer.

Achalasia of the cardia is discussed and the treatment recommended is esophagogastrostomy. The one flaw is regurgitation. The author recommends extramucous esophagocardiomyotomy, which is similar to the Ramstedt operation for hypertrophic pyloric stenosis. In this procedure, the esophagus is freed from the diaphragmatic opening and is pulled down 3 to 4 inches; then a longitudinal incision is made through the last 4 inches of the esophagus, down to the mucosa on the anterior wall and the incision is carried into the cardia for 2 inches and its mucosa exposed. The author advocates wider adoption of this procedure as it is simple and safe; the results, both immediate and late, are very gratifying.

Gastric tumors are thoroughly studied, with emphasis on carcinoma, which comprises 99 per cent of malignant tumors of the stomach. Mr. Maingot feels that although subtotal gastrectomy by one of the Polya technics is the ideal procedure, there are indications for the Billroth I operation. He feels that Billroth I has a lower operative death rate, can be performed in less time than the Polya, and may be applicable in elderly and poor-risk patients.

Total gastrectomy based on the technic of Lahey is fully described and illustrated. The intrathoracic operation is given in detail by Norman Tanner.

The second portion deals with surgical conditions of the spleen. The technic of splenectomy is described, and it is recommended that a small stomach tube be passed preoperatively to insure an empty stomach throughout the operation. Careful search should always be made for accessory splenic tissue and this should be removed.

In the thorough discussion on the pancreas, the author warns of the danger in biopsy of a mass in the head of the pancreas in an effort to determine whether one is dealing with a carcinoma or a pancreatitis. It is easy to injure the duct of Santorini and subsequently develop a pancreatitis or a peritonitis. Injuries may occur on too vigorous palpation or attempted palpation of a stone in the terminal portion of the common bile duct. Gastric and duodenal ulcers which have deeply penetrated the pancreas and are not capable of excision with-

*Abdominal Operations. By Rodney Maingot, F.R.C.S. Eng., Surgeon to the Royal Free Hospital, London and to the Southend General Hospital. Ed. 2. 1,274 pages, 1,051 illustrations including 16 color plates. New York, Appleton-Century-Crofts, Inc., 1948. Price $16.00.

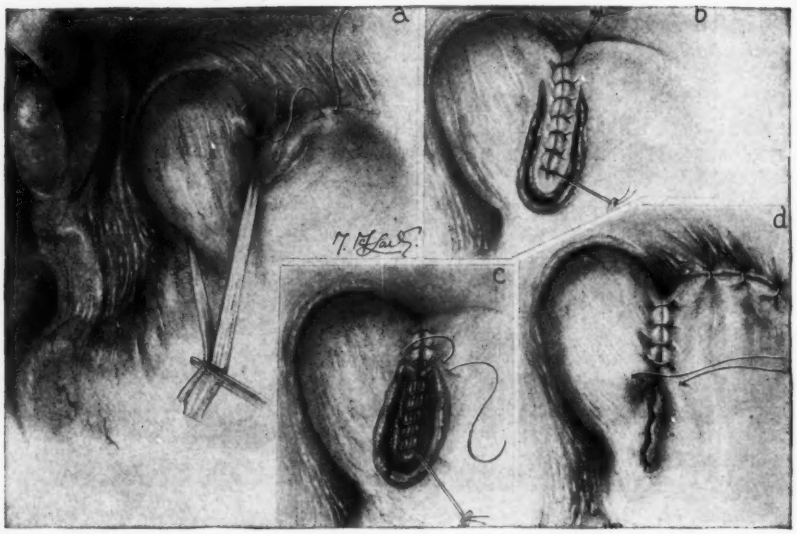


Figure 122. Esophagogastrostomy for cardiospasm (after Clagett).

(Illustrations from Maingot: "Abdominal Operations.")

out injury to the granular tissue are best handled by leaving the base of the ulcer in situ and cutting around it. Cauterization of the base is known to have resulted in pancreatitis or fistula.

In gastric resection for carcinoma and in splenectomy, care must be taken to avoid pancreatic tissue damage. Pseudocysts of the pancreas are best treated by excision, but this is feasible only in a minority of cases. They must either be anastomosed to a loop of proximal jejunum or be marsupialized. The author advocates marsupialization and in the event the fistula fails to close, to implant the fistula into a loop of jejunum. Eighty per cent of cases close spontaneously and in all cases the fluid balance of the patient must be closely watched and the skin protected either by zinc and castor oil paste, kaolin, aluminum paste, or bronze powder, with suction being attached to the fistulous tract.

Acute and chronic pancreatitis are taken up in detail. The treatment recommended, if one can make the diagnosis correctly, is conservative or expectant treatment in acute pancreatitis. In the event surgery is undertaken, local anesthesia is preferred. Any exudate should be aspirated, the gallbladder and ducts examined by sight and touch, the lesser sac opened, and a large rubber tube placed down to the pancreas. The closure recommended is through-and-through interrupted wire sutures.

The author is opposed to any surgery of the gallbladder or extrahepatic ducts even if stones are palpable.

Chronic pancreatitis associated with jaundice is best handled by cholecystojejunostomy and entero-anastomosis. In the event a previous cholecystectomy has been done, the common bile duct should be divided and implanted, end-to-side, in a loop of proximal jejunum and again an entero-anastomosis should be done.

Considerable space is devoted to carcinoma of the pancreas, with the signs, symptoms, and preparation for surgery stressed. The palliative procedures for cases which are found to be irremovable are divided into those treated by external biliary drainage and internal biliary drainage. Cholecystgastrostomy and cholecystoduodenostomy are not recommended. The best measure is cholecystojejunostomy and entero-anastomosis. The outlook is very dim as the operative mortality is 20 to 30 per cent and all patients are dead within one year.

Radical measures for handling carcinoma of the tail and body of the pancreas are discussed. Partial pancreatectomy has rarely been successfully performed. Carcinoma of the ampullary portion and

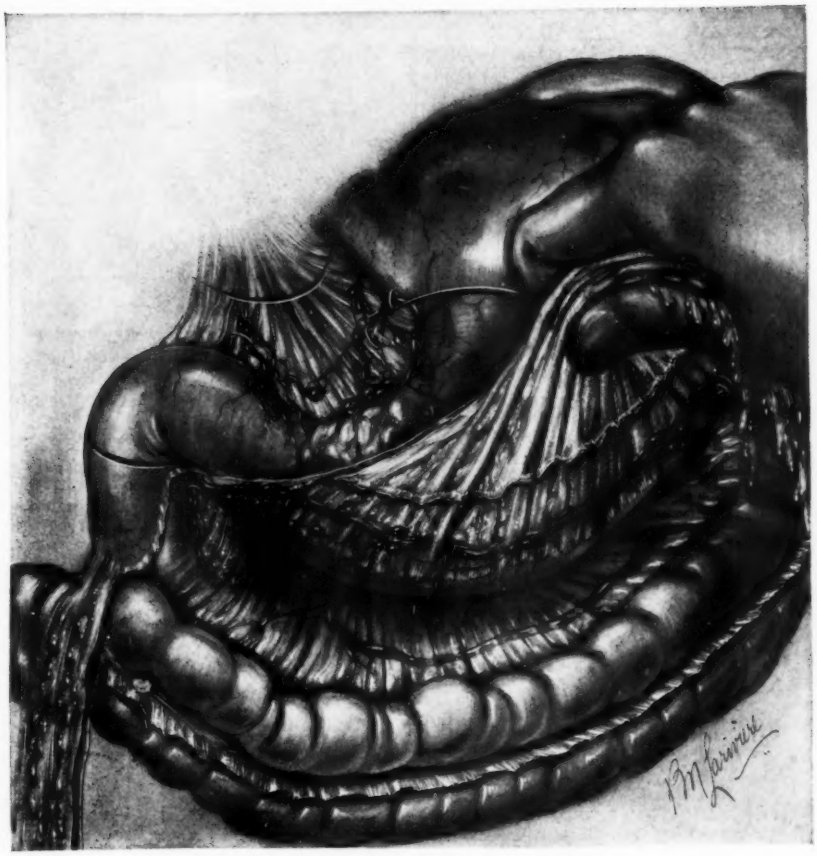


Figure 137. Subtotal gastrectomy. The amount of duodenum, stomach, great omentum, gastrohepatic omentum, glands, etc., which are removed in the operation of subtotal gastrectomy.

the head of the pancreas is handled by either a one- or two-stage procedure. Problems, such as whether the gallbladder should be used to establish bile flow, whether or not to implant the pancreatic duct, are examined, and the technics of one- and two-stage procedures are outlined.

The problem of islet cell tumors and hyperinsulinism is presented. When a patient presents the triad of: (1) attacks of insulin shock coming on during fasting or after exercise; (2) blood sugar of 50 mg. per cent or less; (3) relief of symptoms promptly on ingestion of glucose—Brunschwig advocates exploratory laparotomy for excision of a pancreatic islet cell adenoma. If none is formed, he advocates subtotal pancreatectomy.

The gallbladder and bile ducts are viewed in detail, with description of anomalies of the gallbladder, the duct system, and the blood supply. Injuries to the common bile duct during surgery are emphasized. The author stresses that in stricture of the common bile duct, if end-to-end anastomosis of the common bile duct can be performed, this is the method of choice. When the distal end of the common bile duct cannot be utilized it is better to implant the proximal end into the jejunum rather than into the duodenum. Mucosal approximation is very important and tension must be avoided at the suture line. A T-tube, if used, should be inserted through a separate incision and not brought out through the line of anastomosis.

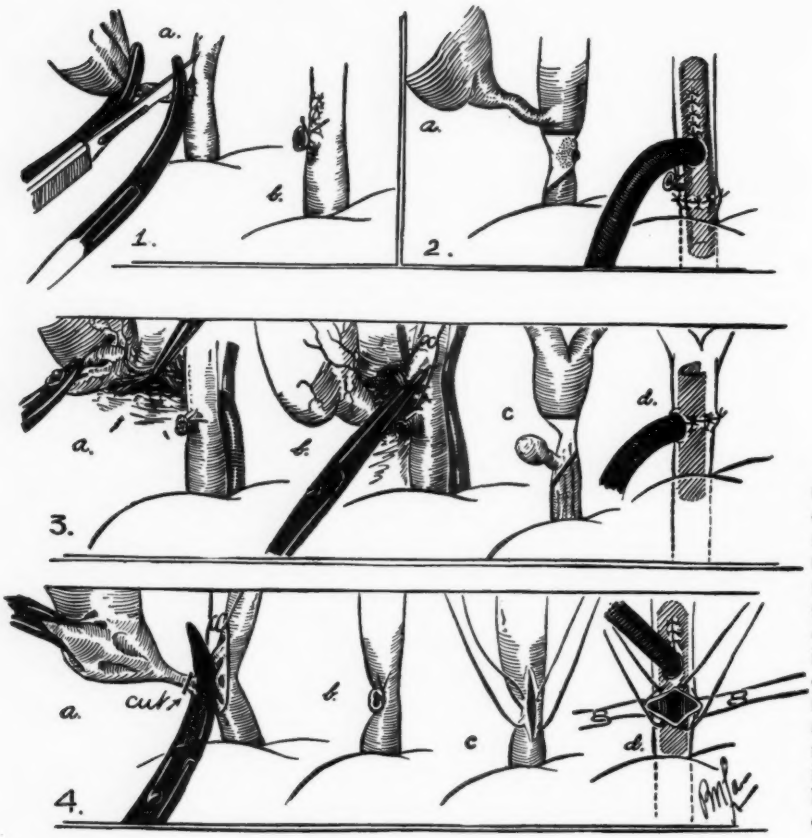


Figure 198. Injuries of the bile ducts during cholecystectomy and the methods of dealing with the strictures which result therefrom. 2. (*a*) shows a stricture produced by a stone which is ulcerating through the common duct and the method of dealing with such a stricture. The method of repair shown in 3(*d*) is incorrect. A better method is depicted in 2.

THE chapter on the liver covers injuries, abscess, tumors and cysts. In dealing with liver lacerations, the author advises suturing; packing is not advised. Resection in cases of massive necrosis of hepatic tissue is the preferred treatment. Drainage should never be omitted. Amebic abscess should be handled medically and the chief indications for surgery are: (1) secondary infection; (2) abscesses which cannot be aspirated by a wide bore needle; (3) large abscesses that do not improve on puncture, and (4) abscesses which have perforated into the abdomen. In pyogenic abscess, the preferred treatment is incision and drainage and avoidance of uninvolved serous cavities.

Benign adenoma is the most common benign tumor of the liver, with lymphangioma, hemangioma, myoma, and teratoma also occurring. Adenoma should be handled by excision. Primary carcinoma of the liver is found in 0.05 to 1.1 per cent of all autopsies. Of the three types—hepatoma, cholangioma, and the mixed type—the hepatoma is the most common. Diagnosis of primary liver tumor may on occasion be made by use of the peritoneoscope. For the diffuse type of primary tumor or for the multiple nodular type, no treatment is of any avail. For the rare cases of solitary accessible primary tumor, resection should be done. Hemostasis is accomplished by compression of the vessels in the free margin of the gastrohepatic ligament, by clamps across the liver, by use of an elastic tourniquet, and the use of oxycel, fibrin foam, etc.

Appendicitis is handled in detail, from the standpoint of etiology, pathology, clinical features, and treatment, including the conservative or expectant

treatment and its indications. The author states that the over-all mortality of acute appendicitis in the United States is about 3 per cent. The subject of peritonitis—acute, secondary, and postoperative—is well handled.

Diagnostic aspiration for a subphrenic abscess should never be done, according to the author. It involves too great a risk of infecting an uninvolved pleura or peritoneum. In doubtful cases, exploratory operation should be carried out. Many cases of subphrenic infection never go on to abscess formation, and conservative management with antibiotics is curative. The extraserous routes should always be employed once drainage becomes obligatory.

The subject of inguinal hernia is treated chiefly from the operative standpoint. In bilateral hernia, it is advised that only one side be done at a time. Simple herniotomy, the Bassini procedure, the Wylls-Andrews imbrication method, Gallie's operation, and the floss silk lattice repair are all described. The latter method is the author's choice and its technic is given in detail. He claims that the all-around recurrence rate using this method is no higher than 3 per cent. It is emphasized that in femoral hernia, the incidence of strangulation is ten times that which occurs in inguinal hernia.

In large bowel strangulation, exteriorization must be done, but primary resection with anastomosis should never be attempted. In small bowel strangulation, resection with primary anastomosis or exteriorization may be done although the former is preferable in the author's experience.

Injuries, both subcutaneous and penetrating, of the small intestine must be treated early. The findings at laparotomy dictate the treatment. Often, closure of a perforation suffices, but in many instances, resection must be carried out. Benign tumors of the small intestine occur about one-third as often as benign tumors of the large bowel while carcinoma of the small bowel is twice as common in occurrence as are benign tumors. Preoperative diagnosis of benign small bowel tumors is rare. Local excision usually is sufficient in these cases, although resection may be necessary when the growth has caused an irreducible intussusception. The prognosis of carcinoma of the small bowel is poor. The five-year cure prospect following resection is no higher than 5 per cent.

Regional enteritis is handled according to the treatment laid down by Crohn and Garlock—i.e., ileotransverse colostomy with transection of the ileum is done where the disease involves the lower reaches of the ileum or if it has spread into the cecum. Ileosigmoidostomy is done if the ascending colon or the transverse colon is involved.

Classification, types and causes, symptoms, signs, and diagnosis of acute intestinal obstruction are all carefully elaborated. General principles and procedures are dealt with in the first portion of this section, while individual obstructive lesions are handled in the latter part. High small bowel obstructions are usually treated conservatively as stoppage is generally temporary and the risk of strangulation is slight. Low small bowel obstruction is very likely to be a strangulation obstruction and laparotomy must be done as soon as the proper preoperative preparation is started.

The subject of diverticulosis, its complications and management, is comprehensively covered. According to the author, about 10 per cent of patients with diverticulitis have complications which require surgical interference. Perforation, abscess formation, obstruction, and colovesical fistula call for operative treatment. Perforation calls for closure of the perforation, drainage of the pelvis and region of the perforation, proximal colostomy and closure of the wound. Localized abscess necessitates drainage but often a fecal fistula results. If obstruction develops, colostomy must be performed. In the event a colovesical fistula develops, a three-staged procedure is required: (1) transverse colostomy, (2) excision of fistula and segmental resection of the diseased portion of colon, and (3) closure of colostomy.

The surgical treatment of ulcerative colitis is necessitated when efficient medical treatment has failed to bring about a cure or produce relief of symptoms, also where a complication occurs such as perforation, abscess, fistula, sinuses, or hemorrhage of polyposis. Appendicostomy is described but is not recommended; volvular cecostomy has no advantage over appendicostomy. Transverse colostomy may sometimes be of benefit when the disease is strictly limited to the rectum and sigmoid. Ileostomy, in various types, is described, the simple loop type being used when the patient is extremely ill. Rankin's technic of single-barreled ileostomy, and the Cattell technic are detailed.

The sigmoid colon is the most common site of cancer of the colon, while the cecum is next in frequency, with the peak incidence occurring from

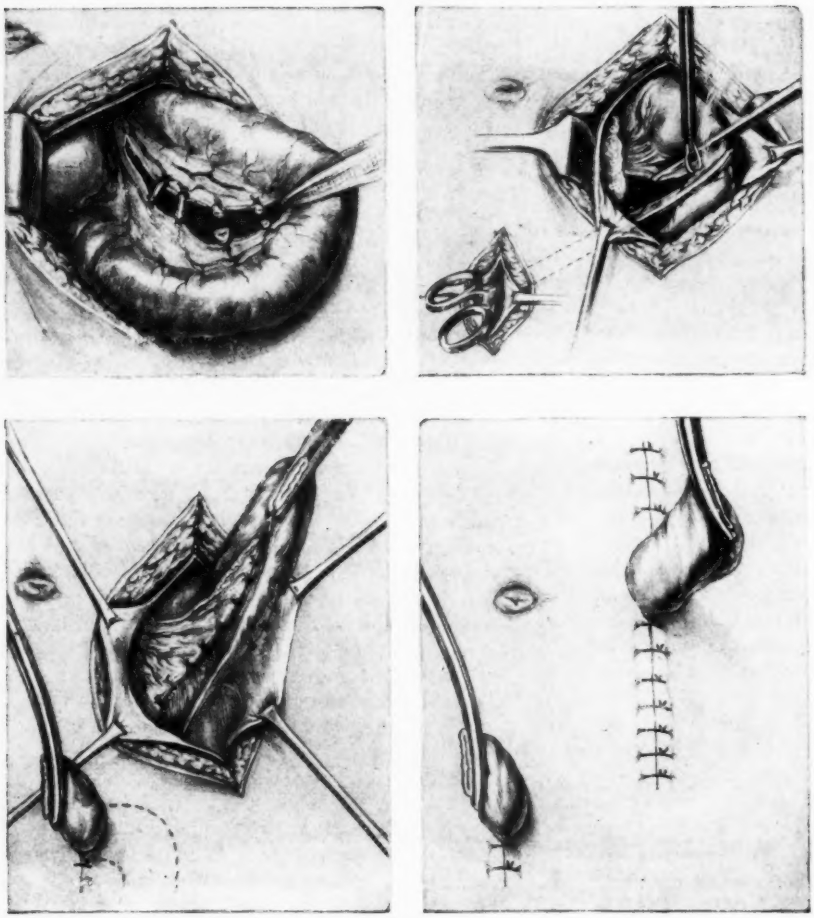


Figure 421. The abdominoperineal resection of the rectum in two stages—Lahey's method. The more important steps in the first stage are illustrated (after Lahey and Cattell).

55 to 65 years of age. The proliferative type is usually seen in the right colon and the annular type in the left colon. Spread occurs by direct infiltration, by invasion of lymphatics and by the blood stream. The prognosis of cancer of the colon as compared to cancer in other parts of the body is favorable.

In cancer of the rectum, 70 per cent of cases involve the upper one-third of the rectum, 25 per cent involve the ampulla, and 5 per cent are situated in the distal portion or anal canal. Their spread is by direct extension, by venous channels and via lymphatics. The operability rate is 80 per cent, being highest in lesions in the lower portions of the rectum and lowest in lesions of the upper one-third of the rectum. Operative procedures in treatment of rectal carcinoma are in general divided into two groups: those with excision and permanent colostomy and those with excision with or without temporary colostomy. A total of thirteen different technics is described.

One complete chapter is devoted to postoperative chest complications, including simple bronchitis, atelectasis, bronchopneumonia, lung abscess, and empyema, with a review of clinical features and diagnosis. Prevention of chest complications is emphasized and pre- and postoperative

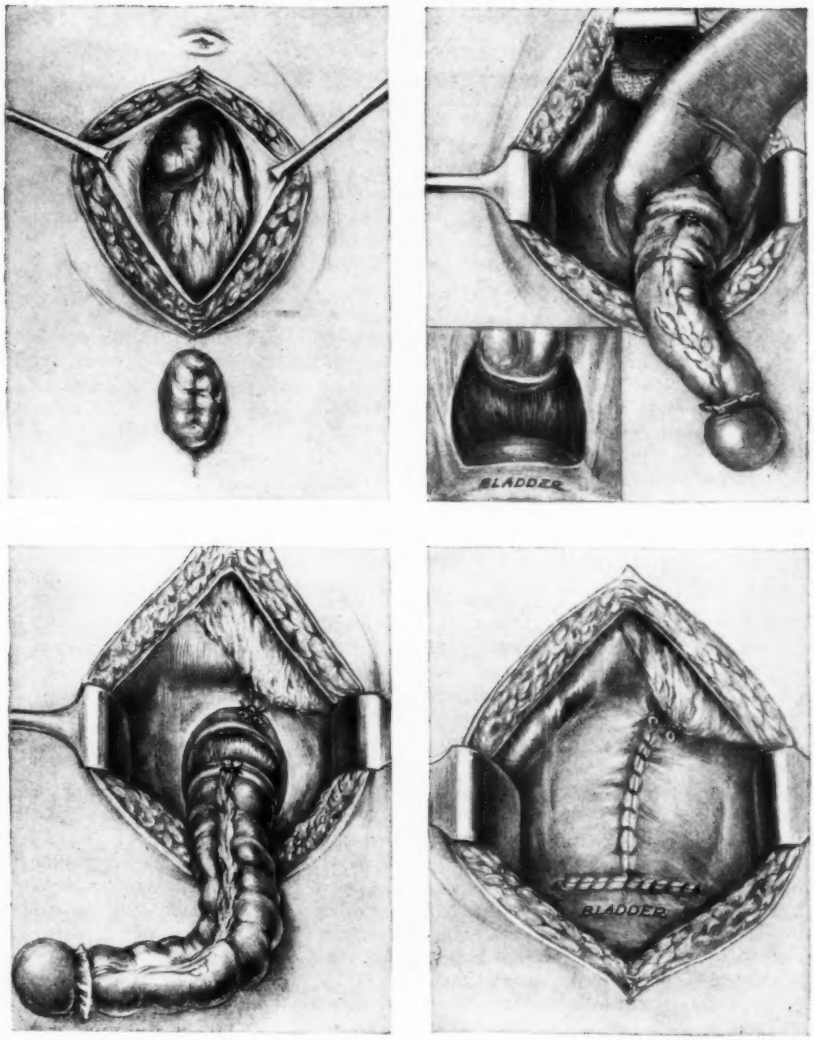


Figure 422. The abdominoperineal resection of the rectum in two stages—Lahey's method. The more important steps of the abdominal portion of the second stage of this method are shown (after Lahey and Cattell).

care of the chest are discussed in considerable detail.

The portion on diaphragmatic hernia is contributed by Harrington and it consists of a comprehensive review of the embryologic aspects, the anatomic aspects, the classification of these hernias, and the general clinical and surgical considerations. Each type of hernia is taken up individually and its clinical aspects and surgical repair are described.

Many more conditions and their surgical treatment are thoroughly discussed in this book, and as this necessarily curtailed review has attempted to show, the volume should be of definite value because of its practicality, readability, and comprehensive review of the major pathologic conditions which are dealt with constantly.

N. B.

New Books Received

► EXPERIMENTAL IMMUNOCHEMISTRY - - -

By Elvin A. Kabat, Ph.D., Associate Professor of Bacteriology, College of Physicians and Surgeons, Columbia University and the Neurological Institute, New York, and Manfred M. Mayer, Ph.D., Associate Professor of Bacteriology, School of Hygiene and Public Health, The Johns Hopkins University, Baltimore. 567 pages. 1948, Charles C Thomas, Springfield, Ill. Price $8.75.

According to the foreword by Michael Heidelberger, Ph.D., Professor of Biochemistry, College of Physicians and Surgeons, Columbia University, though "a complete *Immunochemistry* is yet to be written, the authors have undertaken the major part of the task by assembling for the first time in one place, the scattered technics which have been developed to fill the needs of immunochemical problems as they unfolded, so that knowledge of this complex and widely inclusive field might be advanced. These methods . . . are described in their working details and discussed as to their applicability and limitations" to fill the need of a practical, working text.

► THE RENAL ORIGIN OF HYPERTENSION - - -

By Harry Goldblatt, M.D , Director, Institute for Medical Research, Cedars of Lebanon Hospital; Professor of Pathology, University of Southern California, Los Angeles. A monograph in American Lectures in Pathology, Edited by Paul R. Cannon, M.D., Professor of Pathology, University of Chicago. 126 pages, illustrated. 1948, Charles C Thomas, Springfield, Ill. Price $2.75.

The investigations reported in this book are based on these hypotheses: (1) the part possibly played by the kidney in initiating so-called essential hypertension should be susceptible of experimental investigations; (2) if vascular disease limited to the kidneys, or any other pathologic process capable of producing a similar intrarenal hemodynamic disturbance, be the primary factor in the initiation of essential hypertension, then the production of the counterpart of the physiological effect of such vascular or other renal disease, no matter how it may be accomplished, should result in the development of hypertension; (3) renal excretory functional disturbance should not be a necessary accompaniment of the experimental hypertension.

The book summarizes twenty years of experimental work including discussions of: (1) the production of experimental hypertension; (2) pathologic changes in hypertensive animals; (3) pathogenesis; (4) the humoral mechanism; renin, hypertensinogen, hypertensin and other vasoconstrictor substances; (5) treatment.

► OPIATE ADDICTION - - -

By Alfred R. Lindesmith, Ph.D., Associate Professor of Sociology, Indiana University. 238 pages. 1947, Principia Press, Inc., Bloomington, Indiana. Price $3.00.

In this work, Dr. Lindesmith has emphasized the study of drug addiction as a form of conduct. He has stressed the importance of the difference between *addiction* and *habituation,* and has carefully elaborated on the implications of the distinction. Dr. Lindesmith discusses the physiological, psychological, and sociological factors, showing their inter-relation in the problem of opiate addiction. His investigation includes a great many first-hand interviews with addicts, which give the addict's own impressions of addiction and its effects on him and the society of which he finds himself a member.

► NEUROSURGICAL PATHOLOGY - - -

By Mark Scheinker, M.D., Assistant Professor of Neuropathology and Assistant Professor of Medicine (Neurology), University of Cincinnati. 355 pages, 238 illustrations. 1948, Charles C Thomas, Springfield, Ill. Price $8.75.

This book may be considered a companion volume to the author's textbook on Neuropathology which appeared last year and which deals primarily with medical neurologic disorders. Dr. Scheinker is an expert in his field and has used clinical cases to illustrate his text. The writing is good, and the format, typography, and binding are excellent. The author has discussed the most frequent tumors and omitted detailed descriptions of cellular pathology which cannot be visualized in routine preparations.

The book attempts to present a dynamic approach to the subject and is of interest to neurologists, neurosurgeons, and neuropathologists and general pathologists. It does not, however, cover the field thoroughly enough to fulfill its thesis that it "makes it possible for every neurosurgeon to assume full responsibility of the brain tissue surrounding a tumor" and "is the presentation of a more intimate knowledge of the pathologic reactions for a correct postmortem laboratory examination without special laboratory assistance and without special training in neuropathology."

► DIABETIC MANUAL for the Doctor and Patient - - -

By Elliott P. Joslin, M.D., ScD., Clinical Professor of Medicine, Emeritus, Harvard Medical School; Medical Director, George F. Baker Clinic at New England Deaconess Hospital; Consulting Physician, Boston City Hospital. 8th Edition. 260 pages, illustrated. 1948, Lea & Febiger, Philadelphia. Price $2.50.

In this latest edition of Dr. Joslin's authoritative guide for the diabetic patient and his physician, emphasis has been given to important discoveries such as the new modification of protamine zinc insulin. In many cases, a single injection of this protamine zinc insulin takes the place of two separate injections of crystalline insulin (or regular insulin) and protamine zinc insulin. Also discussed are the significance of uric acid diabetes recently announced by Griffiths of Canberra, Australia, and the new avenues of experimentation which it opens up for a possible prevention of diabetes among relatives, and even the protection of the remaining sound insulin producing cells in the pancreas in the diabetic patient himself. The book is completely up-to-date and 32 pages larger than the previous edition.

► CLINICAL ENDOCRINOLOGY - - -

By Laurence Martin, M.D., F.R.C.P. (London), Physician to Addenbrooke's Hospital, Cambridge, and Martin Hynes, M.D., M.R.C.P. (London), Reader in Medicine in the University of Cambridge. 222 pages, with 8 plates and 22 text figures. 1949, The Blakiston Company, Philadelphia. Price $4.50.

Directed to the general practitioner and the medical student, this book is designed to present a comprehensive account of endocrine disease, emphasizing the physiologic or pathologic basis in each case, and to indicate the limitations of hormone therapy as clearly as its potentialities. The text is divided into ten main sections, each devoted to a separate gland, while the eleventh chapter discusses hormone implantation. Although each subject is covered in its appropriate section, the material is cross-referenced to cover the inter-relationships of endocrine function.

Men of Medicine

A.M.A. HONORS GENERAL PRACTITIONER

In recognition of his thirty-two years of devoted service as a "family doctor" and "father of public health" in the county in which he practices, Dr. W. L. Pressly of Due West, South Carolina, has received the 1948 gold medal of the American Medical Association. Dr. Pressly was selected for the award in final balloting by the House of Delegates of the A.M.A. at the Interim Session of the Association in St. Louis. Two other nominations submitted to the Delegates by the Board of Trustees from the names proposed through county and state medical societies were Dr. Charles Manley Horton of Franklin, Louisiana, and Dr. Lyle Hare of Spearfish, South Dakota.

Dr. Pressly, who gave up a promising career as a professional baseball player in favor of the medical profession, was born in Due West in 1887 and left there only to secure his medical education, internship, and residency. After obtaining his A.B. degree at Erksine College in Due West in 1908, Dr. Pressly received his medical degree from Emory University School of Medicine at Atlanta in 1912 and served as intern and resident at Jefferson Hospital, Roanoke, Virginia, from 1912 to 1915. Before deciding definitely on a medical career, however, he had played first base for the Roanoke minor league baseball team from 1908 to 1913 and was its playing manager in 1912 and 1913. When he checked his balance at the end of his first year of practicing medicine and found that he had earned $750 in contrast to his $5,000 a year baseball salary he "began wondering how I had made such a big mistake."

Not only was his income inadequate, but a country practice in those years involved such physical discomforts as driving a horse and buggy in winter to reach patients in rural sections, and the necessity for treating patients under rather primitive conditions. Many of the 4,200 babies Dr. Pressly has delivered were brought into the world by the light of a kerosene lamp in a farmhouse.

In addition to carrying on his active practice, Dr. Pressly has also participated vigorously in public health campaigns and has sponsored well baby clinics and other measures to help keep his home town people well. He is considered an authority on rural health and sanitation throughout his state.

Dr. Pressly has served as president of the Abbeville County Medical Society and the Third (South Carolina) Medical Society. He was a Councilor of the South Carolina Medical Association from 1933 to 1940, when he was elected president. He was chairman of the General Practice Section of the Southern Medical Association in 1943-44 and is chairman of the South Carolina Academy of General Practice. He has been a member of the executive committee of the South Carolina State Board of Health since 1939, and was state head of the Procurement and Assignment Division of Selective Service during World War II.

In accepting the special gold medal award for a general practitioner who has rendered exceptional service to his community, Dr. Pressly said:

". . . In receiving this honor so graciously bestowed by you, I am deeply appreciative of it. Also, I am greatly indebted to many individuals and organizations for their interest and encouragement.

"I think especially of my own county and state medical associations. For two consecutive years they have seen fit to nominate me for this honor. To these men with whom I have been most intimately associated, my heart goes out in sincere appreciation and love. . . . Also may I be permitted to extend my appreciation and thanks to the Trustees of the American Medical Association on their decision to honor those men who have devoted, and are devoting, their lives to the field of general practice. It has been a great encouragement to the general practitioner to be thus recognized by this organization which we hold in high esteem.

"In entering the field of general practice, I resolved, and have sought rigidly to adhere to, the

E. L. Henderson, of the A.M.A. Board of Trustees, presents General Practitioner Medal to W. L. Pressly.

one idea that my life would be one of service, regardless of any other influence that might come to bear upon it. . . . I am sure this is the desire and ideal of the 100,000 or more general practitioners in our Association. Hence, I regard this honor not as one to me personally, but to me as representing these men and the ideal which we hold dear."

RUNNER-UP IN BALLOTING

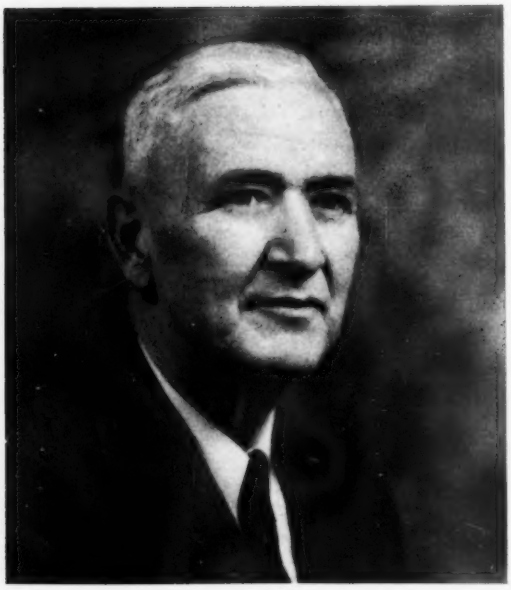
Dr. Hare, the runner-up in the balloting, was born in Cedar Rapids, Nebraska, November 26, 1885. His family moved to Hill City, South Dakota, when he was 4 years old. He graduated from the University of South Dakota in 1907 and from the University of Illinois College of Medicine in 1911, and served his internship at University Hospital, Chicago. He has been a general practitioner in Spearfish for thirty-seven years.

Among the numerous public and professional positions held by Dr. Hare, are secretary and president of his local district medical society and the office of mayor of his community. He served as a captain in the Medical Corps in World War I and was a post commander of the American Legion. Dr. Hare has contributed a considerable amount of his time to the stimulation of the Boy and Girl Scout organizations, the Red Cross, and the growth and improvement of his original alma mater, the Black Hills Teachers' College, which in October 1947, honored him by naming its new stadium "The Lyle Hare Field."

OTHER FINALIST

The third candidate, Dr. Horton, was a telegrapher and train dispatcher in New Orleans before he worked his way through the Tulane University School of Medicine. Born in Lowndesville, South Carolina, in 1879, he is the son of a country doctor. After graduating from Furman University with an A.B. degree, and receiving his M.D. degree from Tulane, he interned at New Orleans Charity Hospital. He began his practice in Franklin, Louisiana

OTHER FINALISTS IN AWARD BALLOTING



LYLE HARE

CHARLES M. HORTON

in September, 1911, and has continued there in general practice to the present time. He has been president of the Louisiana State Medical Association and is a member of the Louisiana Academy of General Practice and the American Academy of General Practice. He is also a member of the Louisiana State Board of Medical Examiners and the Louisiana Physicians' Service.

First established in Chicago in September, 1947, the A.M.A. General Practitioner Award is designated especially to honor a general practitioner who has served as a family physician and who, in that capacity, has received the recognition of his community.

FATHER SCHWITALLA HONORED

At the same time the presentation was made of the general practitioner award, the A.M.A. for the first time in its history awarded a gold medal and citation to a distinguished layman who has served to advance the ideals of American medicine and who has contributed notably to the public welfare. Recipient of this honor was Father Alphonse Mary Schwitalla, whose outstanding career in medical education, public health, and public service was detailed in the biographical sketch about him, published in the January 1948 issue of POSTGRADUATE MEDICINE.

EDITORIALS

ELECTRONARCOSIS

The treatment of various forms of mental illness by physical and pharmacologic means has been used for over ten years. Benefits from these treatments are obtained chiefly in actively psychotic individuals, particularly those suffering from the affective psychoses, both the manic and the depressed types, involution psychoses, and schizophrenia. Handling of the neuroses with these treatments has not been found so satisfactory. A report presented at the American Medical Association meeting in the section on nervous and mental diseases in June, 1948, by Dr. Douglas Goldman, Longview State Hospital, Cincinnati, Ohio, indicates that electronarcosis may offer something in the psychoneuroses which the other forms of physical and pharmacologic treatment cannot achieve.

The report was based upon a mixed group of over 100 patients treated with electronarcosis in the last two years. Most of these were patients who had been subjected to previous forms of treatment for psychotic illness with little or no benefit. A small group of patients suffering from psychoneuroses was included. The patients have not been followed for a period sufficiently long to make the results finally conclusive; but in spite of the fact that the patients chosen for this treatment were those who had failed with previous treatment, the rate of relapse within six months of completing treatment is not more than 2 out of 15. Other patients who are still under observation are reported as "continuing to improve in their social and industrial adaptation in a manner which previous experience with other forms of treatment indicates will continue to be productive and useful."

Electronarcosis has been found most valuable in treatment of affective psychoses, particularly the depressed type of the manic depressive psychosis, and the involution melancholias. Paranoid psychoses of the involution period are also favorably influenced and some of the schizophrenic psychoses are also helped, particularly the catatonic reactions in both the depressed and excited stages. State Hospital patients who are usually suffering from more chronic forms of such illness have responded favorably although not proportionately as well as the private patients. This is to be expected since the duration of illness in such patients and adverse family and environmental conditions made improvement more difficult to obtain. However, several such patients who had apparently been hopelessly ill have been restored to useful living.

A limited number of individuals with psychoneurotic reactions, chiefly evident in compulsive anxiety, repetitious self-disparagement, self-accusation and presence of rigid religious scruples were treated, practically all with considerable relief of these symptoms.

"Apparently, if any one characteristic can be seen which runs through the entire group, both psychotic and psychoneurotic, it is the presence of deep anxiety, otherwise unapproachable by any means whatever. It is such anxiety which electronarcosis alleviates as no other method with the possible exception of lobotomy can," states Dr. Goldman.

The total number of treatments given to in-

dividual patients varied from 12 to more than 30. The first 10 to 12 treatments are given three times weekly, following that the rate is dropped to two weekly and for later "maintenance" treatment, one treatment weekly is often used. Relapses are minimal if such "maintenance" treatment is used following the main course of treatment. This seems to allow patients "to resume normal environmental relationships and responsibilities safely while consequent tensions are continuously dissipated through the treatment as long as they continue to develop. Their development gradually subsides under such technic."

A. E.

THE PSYCHE AND THE SOMA

It seems rather strange that the phrase "psychosomatic medicine" is so commonly found in public prints these days.

As a matter of fact this is no new thing, for every doctor in every generation has come to grips with the disturbed mind in the troubled body. Pierre Janet, famous French writer on neurology, published a book many years ago entitled *Demifous et Demiresponsible* which was, in effect, a treatise on major hysteria. He stated that it is sometimes fairly impossible to separate symptoms due to actual pathology from those which are "thought up" by the patient who looks for sympathy or personal favor through feigned illness. He said also that many operations have been performed on such individuals through mistaken diagnosis because of the misleading "facts" supplied by both subjective and objective evidences.

Dr. J. A. Haiman of New York some twenty years ago, was among the first in America to call attention to symptoms of allergy in the respiratory tract, due to some imbalance in the vegetative nervous system. Not much attention was paid to his articles at that time, but the truth of the statements made then is now being recognized. One begins to query whether there is not "something in this Christian Science business, after all!" Yes, *something* perhaps, but not much from the purely medical and surgical standpoint. You cannot do away with anything by denying its existence. It will arise again and again, though crushed and seemingly annihilated.

Frohman, the Menningers, and many others have emphasized the hereditary tendency to emotional instability in one or both parents. This susceptibility in offspring exists as a body potential which requires only some "trigger mechanism" to set it off.

In the *American Mercury* for May 1948, Dr. Harry Schwartz has written an article of especial value because it explains to the nonmedical person the workings of the psychosomatic complex. As an example he cites a girl aged 8 who was so afflicted with asthma that her mother took her to Florida and remained there with her. During the visit, all signs and symptoms of asthma disappeared, and she seemed well enough to return home. She did so, but the asthma recurred as soon as her brother and sisters came back from camp. It seems that she was annoyed by and bedeviled by these older children, and as a result became bitter, hostile, uncooperative, nail-biting, thumb-sucking and mother-clinging. Sensitivity to dust, certain foods, etc. was present, but this was rather incidental than causative. Mary was an unwanted child, frustrated in her hunger for affection.

A possible explanation of many symptoms may be developed on the basis of stimulation of the fibers of the sympathetic and parasympathetic system thus increasing capillary dilatation and exudation of serum into the surrounding areas. Arteriocapillary pressure is lowered through dilatation of arteriovenous anastomoses. Absorption is retarded by an increase in venous pressure (passive congestion). Absorption is accelerated by increased tissue pressure and lowered venous pressure. The blockage of lymph circulation may become persistent due to fibrosis and interstitial thickening.

We are coming more and more to a consensus that severe grief, anxiety, or severe mental upset from whatever cause fixes the background for varying manifestations of allergy in mucous membranes, and, perhaps, in other tissues as well. But we must be quite sure of

our diagnosis. If the allergic condition is irreversible because of unrequited love, financial reverses or fear in the actual presence of malignant disease, then vaccines from house dust, pollens, animal emanations, protein sensitizations, etc. cannot correct it because they are not the cause. The autonomic stimulations may manifest themselves in skin rashes, gastrointestinal, and other disturbances. Some writers seem to believe that psychosomatic states may have a bearing on arthritic changes because of exudate into capillary areas. This is questionable and requires proof.

We still need all of the armamentarium we can command for the complete analysis of every problem case. There must be no guesswork, or this must, at least, be reduced to a minimum. All laboratory tests, x-rays and other mechanical means must be used, so that nothing is overlooked. Meanwhile we must study the family and individual history of the patient. He or she may "hold out" on us because of some sense of shame or desire to hide certain unfavorable factors which, the patient assumes, "have nothing to do with the case."

Some physicians seem more adept in managing these "psycho cases" than others, possibly because of a warm interest in the patient's welfare which brings out important data. This is psychoanalysis in a sort of revised form. At least part of the answer to the question "Why is So-and-So allergic, while I am not" lies in the psychosomatic makeup—to differences of mental attitude in the presence or absence of the "slings and arrows of affliction."

I. W. V.

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Office Practice

To provide the general practitioner, as well as the specialist, with concise, readily available information on the latest, proved methods of diagnosis and treatment of conditions commonly encountered in an average practice, POSTGRADUATE MEDICINE offers this department to its readers. It is not, of course, intended to present these discussions as the only acceptable therapeutic procedures to be used, but rather to offer simple regimens and recommendations based on the extensive experience of the physicians who prepared these summaries.

CROUP - - -

SIMPLE spasmodic croup is characterized by a rather sudden onset of labored breathing in a susceptible child, usually in the middle of the night. It is more common in winter when the indoor atmosphere is dry and overheated.

Spasm of the larynx is a striking symptom associated with apprehension or fear on the part of the little patient.

The rather dramatic response to an increase in humidity and the comforting embrace of a parent is most helpful from a diagnostic as well as a therapeutic point of view.

The patient's temperature is usually normal. Fever should suggest acute laryngitis or laryngotracheobronchitis.

The pathogenesis of simple spasmodic croup is not fully understood. There appears to be a familial predisposition in many instances. Weather changes often play a role. Signs of mild respiratory disease such as the common cold are frequently associated.

DIFFERENTIAL DIAGNOSIS

This form of croup must be differentiated by clinical and bacteriologic examinations from acute laryngitis, due to the streptococcus, the diphtheria bacillus or other micro-organisms, such as the influenza bacillus, which require more specific forms of therapy.

TREATMENT

Treatment of spasmodic croup consists of removing the child at once to a humid, warm atmosphere. At home this can be accomplished most easily by allowing the hot water tap to run in the bath tub while the patient is reassured.

The temperature of the room should not be over 75° F., however, since excessive heat tends to aggravate the symptoms. For this latter reason, a steam tent is not recommended, except for immediate and temporary relief.

An increase in humidity can usually be maintained by use of a small steam kettle boiling in the child's room. By providing such an atmosphere on the succeeding evening, recurrence of the spasmodic attack can often be prevented.

FOR SEVERE CASES

In the more severe cases, Syrup of Ipecac may be used to relieve laryngeal spasm if given in teaspoonful doses every 15 minutes until emesis occurs. Three drops on the tongue will act as an expectorant and may be helpful when given at two- or three-hour intervals.

Fear is best treated by the patient's being held in the parent's or nurse's arms until the severe spasm stage is over. A small dose of phenobarbital or other mild sedative may be helpful and may be used prophylactically during the period of illness.

The disease rarely lasts more than two or three days, and the symptoms are usually absent during the daytime. The prognosis is excellent, if uncomplicated.

ATHLETE'S FOOT - - -

"ATHLETE'S foot" (tinea pedis) infects over 50 per cent of the population of the United States. Its diagnosis is relatively simple, but its prevention and treatment are rather more complicated.

The layman usually recognizes the disease after he notices the patches of white, sodden epidermis, the fissures, and the blebs between the toes.

When the physician sees the patient, the disease is usually of long standing; it is because of its extension, with new painful lesions, that the patient finally comes to the office. These lesions usually cause burning and itching, and sometimes they are secondarily infected and exhibit the characteristic findings of inflammation due to pyogenic cocci.

TREATMENT

For treatment of these active lesions, the best fungicides are benzoic acid, salicylic acid, sulfur, and the newer preparations of proprionic acid and undecylenic acid.

The old reliable, Whitfield's ointment (one-half strength), can be put to good use in this condition, applying one application each night, and later one application weekly to offset a recurrence.

In recent years, a talcum powder containing 2 per cent undecylenic acid and 20 per cent zinc undecylenate has become very popular.

It should be remembered that if the lesions are of the dry, thick, keratotic type, strong keratolytic agents, such as salicylic acid, should be used. However, if there are acute, red, vesiculated lesions, one must not be too aggressive and either a 1:4,000 potassium permanganate soak, or an aqueous Gentian violet painting should be applied.

PROPHYLACTIC TREATMENT

No active therapy of "athlete's foot" is effective unless prophylactic treatment is also followed. Fungi like soggy moist skin; hence careful drying of toes and feet is essential.

The patient should change socks daily, and preferably wear light weight wool socks. Shoes and socks should be well aired when not in use.

For those who have hyperhidrosis, a foot powder such as alum foot powder is recommended. This contains equal parts of potassium alum, zinc oxide, bentonite, and talcum powder.

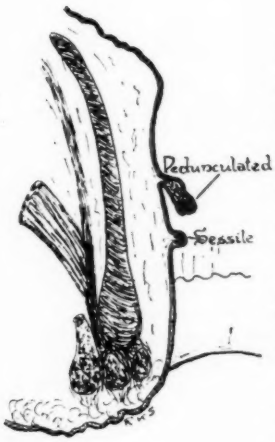
Naturally attempts must be made to avoid contact of the naked foot with the fungus, which is apt to be present in showers, locker rooms, gymnasiums, and the like. Thus, the feet should be covered or protected in these places.

Finally, careful foot hygiene, including properly fitting shoes, and avoidance of blisters and erosions are essential in offsetting a fungus infection.

USE OF SIGMOIDOSCOPE - - -

THE adage, *"If you don't put your finger in the rectum, you put your foot in it,"* must now be modified. You must put in not only the finger, but also the sigmoidoscope.

It has been stated recently in cancer detection clinics that one of the most valuable single diagnostic procedures in the entire clinic is sigmoidoscopy. Frequently, in fact, this is the only way that one can diagnose an early ulcerating colitis.



From: "Essentials of Clinical Proctology," by Manuel G. Spiesman and Anthony Bassler. Grune & Stratton, New York, 1946.

Proctoscopy and sigmoidoscopy are of utmost importance in routine examinations of patients in the office.

Cancer of the large intestine supplies about 8 per cent of all carcinomas and over half of these are found in the rectum and sigmoid. And it must be realized that many cancerous and precancerous lesions in this area can only be diagnosed with a sigmoidoscope. Many are out of reach of the examining finger or are too small or too soft to be felt. This is especially true of tiny polyps and adenomas.

The significance of polyps and adenomas can not be overemphasized, and their prompt biopsy and removal is imperative. Some proctologists claim that 40 to 50 per cent of such growths become malignant.

Also it should be noted that a negative barium x-ray study of the rectum and sigmoid is not conclusive. As far as the x-ray is concerned, there are many "blind-spots" in this area where these tumors may be "hiding."

The technic and performance of proctoscopy and sigmoidoscopy are easily adapted to office practice. The patient is instructed to have an enema the preceding night, and sufficient enemas the following morning until the returns are clear.

THE EXAMINATION

The examination is done with the patient placed in the knee-chest position. Fancy, expensive tilt-tables are not necessary.

First, digital and proctoscopic examinations are done. Then the sigmoidoscope is inserted, and its passage is performed under direct vision with the help of very gentle insufflation. Of course, one should be thoroughly familiar with the normal gross anatomy of the recto-sigmoid before attempting this procedure.

A cursory examination of the bowel is made as the instrument is inserted and a more thorough examination is made as it is withdrawn.

POINTS TO OBSERVE

One must observe carefully the mucosa. Is it normal, atrophic, or hypertrophic, pale or hyperemic? Are there hemorrhoids, ulcers, strictures, tumors, etc. present? Unlimited information may be gained in answering these questions.

The value of sigmoidoscopy is obvious and since it is relatively simple to do, the routine use of the sigmoidoscope in the office is strongly recommended.

Consultation Service

This special consultation information service is offered as a regular monthly feature of *Postgraduate Medicine*. Readers are invited to call on this Service for answers to difficult medical problems from members of our Editorial Board best qualified to help. Each question will be answered by mail and those of general interest will be published each month. Address all communications to Consultation Service, *Postgraduate Medicine*, 516 Essex Building, Minneapolis 3, Minnesota.

DICUMAROL

QUESTION: What is the present status of the use of dicumarol in the treatment of coronary thrombosis?
M.D.—Michigan

ANSWER: The use of this anticoagulant has four principle objectives: (1) prevention of extension of the thrombus in a coronary artery; (2) prevention of the formation of mural thrombi; (3) prevention of venous thromboses and secondary embolism; and (4) prevention of peripheral arterial thrombosis in vessels already the site of atherosclerosis.

Present usage indicates that the optimal prothrombin level is 10 to 30 per cent that of normal plasma and that in the majority of cases this is a safe procedure. The highest incidence of thromboembolic phenomena in untreated cases ranges from the fourth to the twentieth day. It is therefore important that the decision to use dicumarol be reached as early as possible and the anticoagulant be given preferably within forty-eight hours of onset.

The status of the preliminary or simultaneous use of heparin is not yet definitely established: some use it only when the development of shock may be expected to encourage the extension of thrombosis in the coronary arteries; others use it routinely. The usual preliminary dose of dicumarol is 200 to 300 mg. orally with subsequent daily dosage regulated by the daily determination of prothrombin time. Some difficulty may be found maintaining the optimal prothrombin level over the usual course (twenty-five to thirty days).

Dicumarol should not be used without adequate laboratory control. Where the use of heparin is decided upon, several methods are available: (1) slow intravenous drip (300 mg. of heparin to a liter of 5 per cent glucose in water continuously at a rate of 20 drops per minute); (2) intermittent intravenous injection of 50 mg. every four hours; (3) the administration of heparin intramuscularly in slowly absorbed media. Heparin administration must be controlled by determinations of the clotting time (capillary method) every four hours.

Bleeding is the only complication noted. This may occur as a hematoma of joints, as epistaxis, hematuria, subarachnoid hemorrhage, or gastrointestinal bleeding. Therefore, the presence of renal or hepatic pathology, known gastrointestinal ulceration, or engorgement (such as hemorrhagic gastritis) should be looked upon as a contraindication for the administration of anticoagulation therapy.

There is reason to believe that dicumarol will not cause the development of subintimal hemorrhage in the coronary arteries, that it will not interfere with the healing of myocardial infarction, and that it will not encourage myocardial rupture. (Incidence of rupture is approximately 10 per cent in untreated cases.)

Anticoagulant therapy will not influence the mortality where there is extensive enough infarction to kill in a few hours or days. The reduction in deaths is in those surviving the acute phase of myocardial infarction in whom secondary thrombo-embolic phenomena are common and not infrequently determine survival.

Anticoagulant therapy should not be used without preliminary determination of the prothrombin time (it may already be low), and without good presumptive evidence supporting a diagnosis of myocardial infarction. (N.B. similarity of clinical picture of infarction to that of gastrointestinal bleeding, including electrocardiographic changes due to myocardial ischemia).

W. S. McCann

THIOURACIL IN TREATMENT OF THYROTOXICOSIS

QUESTION: What is the status of thiouracil preparations in the treatment of thyrotoxicosis?
M.D.—Illinois

ANSWER: Thiouracil is too toxic to be used safely in the treatment of thyrotoxicosis. Propyl thiouracil has been proved to be quite safe and no deaths have been reported following its use. It is an effective means of preparation of patients for thyroidectomy, or of controlling hyperthyroidism indefinitely in patients who are poor surgical risks.

In about 50 per cent of the patients who have relatively small thyroids and mild to moderate hyperthyroidism, prolonged treatment with propyl thiouracil over a period of from six months to a year will result in a prolonged remission of the hyperthyroidism following withdrawal of the drug. Many of these patients appear to be cured as effectively as by thyroidectomy, but sufficient time has not as yet elapsed to enable us to evaluate the ultimate results.

It is generally conceded that nodular goiter with hyperthyroidism should be treated by thyroidectomy, except in the older age groups, where the risk of operation is increased. Attempts to effect a definitive cure with propyl thiouracil should be limited to those patients with Graves' disease, small goiters, and mild to moderate hyperthyroidism.

George Crile, Jr.

INFECTIOUS MONONUCLEOSIS

QUESTION: Would appreciate any recent information as to etiology and treatment of infectious mononucleosis.

M.D.—Illinois

ANSWER: Infectious mononucleosis is a disease of unknown etiology that is characterized by fever, malaise, adenopathy, and usually by an increase in the leukocyte count. Morphologic examination of the smears reveals lymphocytosis, usually with mature cells present. Although these cells are atypical, they rarely are immature.

Since infectious mononucleosis is a self-limited disease and practically never proves fatal, palliative treatment for the fever and irritation in the mouth and throat as a rule will suffice.

For more detailed information in regard to infectious mononucleosis, the inquirer is referred to three articles in the August issue of *Blood*, 1948, Vol. 3, No. 8, entitled "Infectious Mononucleosis," by Sir Henry Tidy; "The Pathology of Infectious Mononucleosis," by Custer and Smith; and "Chronic Infectious Mononucleosis," by Raphael Isaacs.

TONSILLECTOMY FOR RHEUMATIC FEVER PATIENT

QUESTION: Would it be advisable or not to remove the tonsils of a 9-year-old white girl who has been suffering from acute rheumatic fever with cardiac complications for the past six months? This girl's tonsils appear to be chronically inflamed and I do not believe her condition is going to improve despite the usual accepted procedures of treatment in the presence of these tonsils. Prior to removal I planned to administer heavy dosages of penicillin and sulfa drugs and maintain these drugs at a high level until complete healing takes place.

M.D.—Kansas

ANSWER: It is generally accepted as good practice to remove tonsils and adenoids from a child who has rheumatic fever; this should be done in a quiescent period. Kaiser, however, concludes "when a rheumatic infection has once manifested itself, tonsillectomy does not safeguard the child against recurrent attacks." Chemotherapy as suggested just prior to, and for a short period after, operation, is advisable.

REFERENCE

KAISER, A. D.: Children's tonsils in or out; a critical study of the end results of tonsillectomy. Philadelphia, J. B. Lippincott Company, 1932, p. 163.

CHRONIC LYMPHATIC LEUKEMIA

QUESTION: What are the effects of urethane and radioactive preparations in the treatment of chronic lymphatic leukemia?

M.D.—New York

ANSWER: Urethane was first introduced, in the control of blood dyscrasias, by Dr. Edith Patterson, in England, and her report[1] shows that its greatest use is in the control of chronic myelogenous leukemia. Her experience with chronic lymphatic leukemia was quite unsatisfactory, and less than one-third of the cases showed a clinical remission. Experience of others confirms this. Occasionally, one sees a decrease in the lymphocytosis and resolution of lymph nodes and splenomegaly, but this reaction is transient and unpredictable.

Radioactive phosphorus is the only isotope of practical therapeutic importance. Its localization is greatest and most constant in the bone marrow, and variable in the lymph nodes and the spleen. It, therefore, is less efficacious in chronic lymphatic leukemia, and in the myeloid type. Reinhard[2] and others recently reviewed the experience at Washington University, and report that approximately 50 per cent of the cases of chronic lymphatic leukemia had a good therapeutic response. It is their feeling that radioactive phosphorus is as satisfactory, but no better than x-ray radiation in relieving the symptoms and prolonging life.

In general the response of chronic lymphatic leukemia to all therapeutic agents depends upon the type and stage of the disease and the age of the patient. The most satisfactory therapeutic response is seen early in the course of the disease and in the aged individual, with small lymphocytes in the peripheral blood. Experience has established local roentgen therapy as the most valuable treatment in the control of chronic lymphatic leukemia.

SUGGESTED READING

1. PATTERSON, E., HADDOW, A., THOMAS, I., and WATKINSON, J. M.: Leukemia treated with urethane, compared with deep x-ray therapy. Lancet 1:677 (May 11) 1946.
2. REINHARD, EDWARD H., MOORE, CARL V., BIERBAUM, OLGA S., and MOORE, SHERWOOD: Radioactive phosphorus as a therapeutic agent. A review of the literature and analysis of the results of treatment of 155 patients with various blood dyscrasias, lymphomas, and other malignant neoplastic diseases. J. Lab. & Clin. Med. 31:107, 1946.

UNDULANT FEVER

QUESTION: Have you any new suggestions for treatment of undulant fever or chronic paratyphoid?

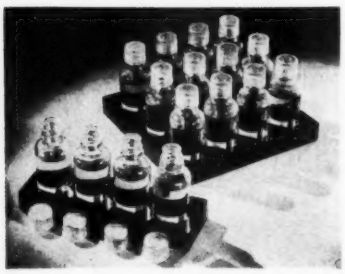
M.D.—Idaho

ANSWER: In spite of much investigative work there is no specific treatment available for undulant fever. On the other hand, in the treatment of acute undulant fever, best results can be expected when a combination of streptomycin and sulfadiazine is used according to the recommendation by Pulaski and Amspacher (Streptomycin therapy in brucellosis. Bull. U.S. Army M. Dept. 7:221-225, February 1947).

There is nothing new available for the treatment of chronic paratyphoid.

New Drugs and Instruments

Information published in this department has been supplied by the manufacturers of the products described.



LA MOTTE COPPER SULFATE SPECIFIC GRAVITY OUTFIT

PURPOSE: Determination of specific gravity of the blood, and from it the hemoglobin content. Also to determine total protein concentration by examining the serum or plasma of blood in the same manner.

DESCRIPTION: The Outfit consists of 16 standard solutions with gravity intervals of 0.004, covering the range from 1.016 to 1.076, contained in screw cap bottles, mounted on movable racks. Full instructions furnished for making the test.

PRODUCER: LaMotte Chemical Products Co., Baltimore 4, Md.

STATICIN CARONAMIDE

PURPOSE: A compound for use concomitantly with penicillin.

COMPOSITION: Caronamide is the short common name for 4′ carboxyphenylmethanesulfonamide.

INDICATIONS FOR USE: Particularly effective in the treatment of conditions that require high and sustained levels of the antibiotic such as typhoid fever, osteomyelitis, and subacute bacterial endocarditis. The drug acts temporarily to inhibit the excretion of penicillin through the little tubes in the kidney and this retains a higher concentration of penicillin in the blood streams for longer periods of time.

DOSAGE AND ADMINISTRATION: Staticin Caronamide is administered orally in orange juice, milk, water, or any other suitable vehicle. Recommended dosage is 1.5 gm. to 3.0 gm. (3 to 6 tablets) every three hours or 2.0 gm. to 4.0 gm. (4 to 8 tablets) every four hours in conjunction with penicillin. It should be administered at intervals no greater than four hours regardless of the interval or route of penicillin dosage. Dosage varies for patients over 60 and patients of younger ages.

HOW SUPPLIED: In 0.5 gm. tablets, bottles of 100 and 1,000.

PRODUCER: Sharp & Dohme, Inc., Philadelphia 1, Pa.

SUSPENSION RESTROL

PURPOSE: Sterile suspension of microcrystalline Dienestrol in normal saline, for the treatment of menopausal syndrome, amenorrhea, suppression of lactation, and hypoovarian states.

COMPOSITION: Microcrystals of Dienestrol, ranging from 3 to 5 microns in diameter, suspended in normal saline. When well shaken, the suspension uniformly contains 5 mg. of Dienestrol per cc.

CAUTIONS: A personal or familial history of malignancy of the reproductive organs is a contraindication to treatment with Restrol.

DOSAGE AND ADMINISTRATION: For treatment of menopausal syndrome: 2.5 to 5 mg. (½ to 1 cc.), injected intramuscularly once or twice weekly. Suppression of lactation: 5 to 10 mg. (1 to 2 cc.), injected intramuscularly once each day for three to four days. Injections should be made intramuscularly in either the deltoid or the upper outer quadrant of the gluteal area, using a 22-gauge 1½ inch needle. After insertion of the needle, the plunger of the syringe should be slightly withdrawn; if no blood is aspirated, Restrol may be injected.

HOW SUPPLIED: In multiple-dose vials of 10 cc. (containing 5 mg. Dienestrol per cc. when entirely suspended).

PRODUCER: Central Pharmacal Company, Seymour, Ind.

CHORIONIC GONADOTROPIN

DESCRIPTION: A purified chorionic gonadotropin in stable, lyophilized dry form.

INDICATIONS FOR USE: In the male, stimulates the interstitial cells of the testis to increased formation of androgens which promote growth and development of secondary sex organs, including descent of the testes. In the female, may affect functional uterine bleeding and secondary amenorrhea and oligomenorrhea but is ineffective in uterine bleeding due to organic causes and in primary amenorrheas. For use in treatment of cryptorchidism not due to anatomic obstruction; in treating adiposogenital dystrophy in boys; in the management of functional uterine bleeding and secondary amenorrhea and oligomenorrhea.

DOSAGE AND ADMINISTRATION: Intramuscularly, for cryptorchidism 50 to 100 I.U. 3 times weekly, increased to 300 I.U. 3 times weekly; in male hypogonadism increased to 500 to 1,000 I.U. if required. In functional uterine bleeding, 200 to 500 I.U. daily for several days prior to expected onset of bleeding.

CAUTION: Excessive therapy in boys may induce precocious puberty.

HOW SUPPLIED: Ampules, 5,000 I.U., with accompanying vial of sterile distilled water for solution prior to injection.

PRODUCER: The Armour Laboratories, Chicago 9, Ill.

MORUSUL

PURPOSE: Sclerosing treatment of varicose veins.

COMPOSITION: Sodium morrhuate 5 per cent and sodium sulfadiazine 10 per cent.

DESCRIPTION: Morusul is designed to simplify the sclerosing treatment of varicose veins. The addition of sodium sulfadiazine changes the physical properties of the solution so that a firmer and more adherent clot is formed.

HOW SUPPLIED: 25 cc. multiple dose vial.

PRODUCER: Endo Products, Inc., Richmond Hill, N.Y.

SYRUP CHOLINE BICARBONATE

PURPOSE: For treatment of fatty infiltration of the liver and hepatic cirrhosis.

COMPOSITION: Contains 17 per cent (w/v) choline bicarbonate in aqueous solution, and presents the equivalent of 12.5 per cent choline base or 14.4 per cent choline chloride.

DOSAGE AND ADMINISTRATION: As much as 20 gm. of choline equivalent may now be given daily. These larger quantities appear to exert a beneficial action on atherosclerosis.

PRODUCER: C. S. C. Pharmaceuticals, Terre Haute, Ind.

ETAMON CHLORIDE

PURPOSE: Ganglionic blocking agent.

COMPOSITION: Etamon Chloride (tetraethylammonium chloride, P. D. & Co.) is a quaternary ammonium compound which reversibly blocks transmission of the motor impulses of both the sympathetic and parasympathetic divisions of the autonomic nervous system. It has a *p*H of 6 and is chemically stable.

INDICATIONS FOR USE: Diseases in which Etamon has been used include: thromboangiitis obliterans (Buerger's disease), arteriosclerosis obliterans, various causalgias including reflex dystrophy, thrombophlebitis, Raynaud's phenomenon, trenchfoot, and immersion foot.

CAUTIONS: Etamon should be used with caution in patients with severe hypertension, particularly in the presence of poor renal function or a high diastolic pressure. It is not advisable to give repeated injections to those patients who have impaired renal excretion. Should not be used in cases with a recent coronary thrombosis, and should be used with caution in elderly and arteriosclerotic patients who will often experience a severe decrease in blood pressure and a diminution in blood flow in their legs during the hypotension. Patients must be kept in a recumbent position for one hour following administration in order to avoid postural hypotension.

DOSAGE AND ADMINISTRATION: Intravenous injection of from 2 to 5 cc., representing 0.2 to 0.5 gm. of tetraethylammonium chloride, is generally employed. In patients under marked nervous tension, no evaluation should be made until the patient has had at least three injections. Intramuscularly one may give from 10 to 12 cc. (5 to 6 cc. in each buttock) of the solution, depending on the body weight, but the dose should not exceed 20 mg. per kg. of body weight.

HOW SUPPLIED: Available in 20-cc. Steri-Vials containing 0.1 gm. of the drug per cc.

PRODUCER: Parke, Davis & Company, Detroit, Mich.

PNEOPHORE

PURPOSE: Treatment of respiratory ailments in which the lungs or parts of the lungs are inactive.

DESCRIPTION: The Pneophore administers oxygen under intermittent positive pressure only. The oxygen delivery pressure is adjusted by a regulator to that recommended by the physician.

The apparatus has six main components: a high pressure reducing valve to reduce the pressure of oxygen leaving the cylinder to 50 pounds per square inch and a gauge to indicate oxygen cylinder pressure; a low pressure regulator reduces 50 pounds per square inch to an adjustable pressure range from 0 to 30 cm. of water; a gauge calibrated in centimeters of water; a six-foot rubber tubing leading to the differential pressure valve. This valve acts as a respirator, converting a continuous positive pressure into intermittent positive pressure. Two different size positive pressure facepieces, each with a four-inch attached tubing, complete the assembly.

PRODUCER: Mine Safety Appliances Co., Pittsburgh, Pa.

DECAPRYN

PURPOSE: Antihistaminic preparation.

COMPOSITION: Each scored tablet contains 25 mg. of Decapryn, brand of Doxylamine, Succinate.

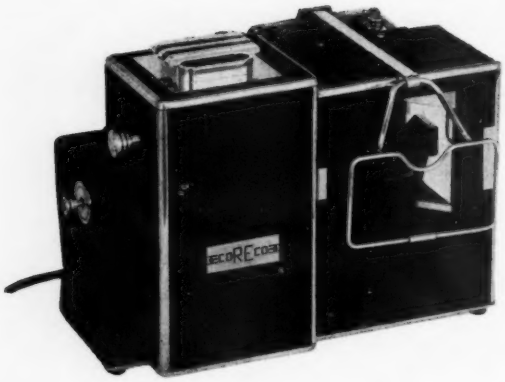
DESCRIPTION: Antagonizes the effect of histamine and counteracts certain allergic and anaphylactic phenomena. Relieves sneezing, rhinorrhea, nasal obstruction and itching of the nose and eyes in allergic rhinitis and hay fever and the pruritus associated with urticaria, atopic eczema, and drug rash. Relieves some of the minor symptoms of bronchial asthma. In clinical tests it produced side actions in less than 10 per cent of patients.

INDICATIONS FOR USE: Allergic rhinitis, hay fever, urticaria, angioneurotic edema, atopic dermatitis, drug rash, dermographism, serum sickness, and certain cases of bronchial asthma.

DOSAGE AND ADMINISTRATION: 12.5 mg. to 25 mg. (½ to 1 tablet) repeated every four to six hours as needed.

HOW SUPPLIED: Bottles of 100 and 1,000.

PRODUCER: The Wm. S. Merrell Company, Cincinnati, O.



CORECO AUTOMATIC COLOR CAMERA

DESCRIPTION: The Coreco Camera is designed to photograph all surface areas of the body—from 1-to-1 close-up pictures to half-body size—and all cavities of the human body, such as mouth, throat, ear, nose, vagina, and rectum. The camera carries its own specially developed, fully color-corrected bulb and a mechanism for complete control of its color temperature and exposure within the camera itself. There is an automatic view finder synchronized with the automatic camera mechanism to permit viewing until a fraction of a second before exposure. The camera provides for automatic focusing.

An x-ray film applicator is included, making it possible to record all sizes and densities of x-ray film on Kodachrome transparencies.

PRODUCER: Coreco Research Corporation, 1908 Broadway, New York 23, N.Y.

AMETHONE AND NEMBUTAL

PURPOSE: In the treatment of spasms of the gastrointestinal tract.

DESCRIPTION: Amethone is the Abbott registered trade mark for a new synthetic compound having an antispasmodic action on smooth muscle in many organs, especially those of the genitourinary and gastrointestinal tract. While Amethone is only about 1/10 to 1/20 as potent an antispasmodic agent as is atropine, it is only about 1/100 as likely to produce the undesired side effects of pupillary dilatation and drying of salivary secretions. In combination with Nembutal, the antispasmodic effect of Amethone is appreciably prolonged, and certain undesired side-effects are mitigated. Each capsule contains Amethone Hydrochloride, 50 mg., and Nembutal, 15 mg.

INDICATIONS FOR USE: In addition to being used in the treatment of spasms of the gastrointestinal tract such as cardiospasm, it may be used for pain due to spasm connected with gastric and duodenal ulcer, spasm of the gallbladder and bile duct, and spasm of the colon. In some cases Amethone and Nembutal may afford relief for patients with moderate asthma and with dysmenorrhea.

DOSAGE AND ADMINISTRATION: The recommended dose for the treatment of spasms of the gastrointestinal tract is 1 to 2 capsules of Amethone and Nembutal every three hours, to be continued as needed, but not longer than two weeks at a time.

HOW SUPPLIED: As capsules in bottles of 100.

PRODUCER: Abbott Laboratories, North Chicago, Ill.

MICROPELLETS PROGYNON

PURPOSE: Estrogen therapy.

DESCRIPTION: Alpha-estradiol provides follicular hormone where there is depressed, insufficient or absent ovarian estrogenic activity. The action of Micropellets Progynon results from the rapid absorption of the saline solution and the establishing of a depot of alpha-estradiol in the tissues from which absorption begins promptly and continues for a long period.

COMPOSITION: Alpha-estradiol, U.S.P. XIII, the pure microcrystalline follicular hormone, in aqueous suspension.

INDICATIONS FOR USE: Menopause, secondary amenorrhea due to depressed ovarian function with inadequate production of estrogenic hormone, hypogonadism, complete absence of follicular hormone resulting from x-ray or surgical castration.

DOSAGE AND ADMINISTRATION: One mg. (12,000 R.U. or 120,000 I.U.) once or twice weekly, which may later be reduced to 1 mg. weekly or even 0.5 mg. weekly.

HOW SUPPLIED: Multiple dose vials of 10 cc., containing 1 mg. (12,000 R.U. or 120,000 I.U.) per cc. Boxes of 1 to 6 vials.

PRODUCER: Schering Corporation, Bloomfield, N.J.

BUTANEFRINE

PURPOSE: For effective bronchodilatation without significant pressor action.

COMPOSITION: Butanefrine hydrochloride, racemic 1-(3,4-dihydroxyphenyl)-2-amino-1-butanol hydrochloride, is a synthetic sympathomimetic drug.

DESCRIPTION: Colorless, odorless, crystalline powder with a bitter taste. Readily soluble in water and alcohol; insoluble in ether and benzene. Melts with decomposition at 198 to 200° C.

INDICATIONS FOR USE: Bronchial asthma. Gives relief equal to that of epinephrine in most patients, with fewer and less marked subjective side effects, such as precordial pain, nausea and vomiting, excitation, and apprehension.

DOSAGE AND ADMINISTRATION: Administered subcutaneously and intramuscularly, intravenously only in emergencies and with caution. The average adult dose is 1 cc. of 1:500 solution (2 mg.). Children are given proportionately less, from 0.5 to 0.8 cc. (1 to 1.6 mg.), depending on age. Intravenously, from 0.5 to 2.5 cc. (1 to 5 mg.) are injected very slowly over a period of from seven to ten minutes; rarely, up to 5 cc. (10 mg.) may be indicated for an adult.

HOW SUPPLIED: Aqueous solution 1:500 (0.2 per cent solution) in ampules of 1 cc. (2 mg.), boxes of 10 and 25; also in rubber diaphragm stoppered vials of 30 cc. (2 mg. per cubic centimeter).

PRODUCER: Winthrop Chemical Company, Inc., New York 13, N.Y.